



Pallierende kemoterapi og targeteret behandling til patienter med bløddelssarkom

Version 2.0

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Nyt siden sidst (ændringslog)

Retningslinjen er kritisk gennemlæst af arbejdsgruppen og anbefalinger og indhold er vurderet gældende.

Nyt siden version 1.2

Retningslinjeafsnit	Beskrivelse af ændring
Titel	Ændret til " Pallierende kemoterapi og targeteret behandling til patienter med bløddelsarkom"
Litteratur- og evidensgennemgang	Der er foretaget en opdateret litteratur gennemgang indenfor alle anvendte behandlings områder og nye studier er inkluderet i evidensstaberne. Der er ligeledes foretaget en litteratur gennemgang af immunterapi, således at dette nu også er inkluderet i retningslinjen.
Bemærkninger og overvejelser	Immunterapi er som noget nyt blevet inkluderet. Dertil kommer en uddybelse af kliniske forsøg og målrettet behandling, da dette fylder mere og mere for vores patientgrupper og fordi sarkompatienterne er blevet udvalgt til at kunne få fortaget omfattende genetiske sekventering. Et fase III studie har konkluderet at der ikke er en effekt af kombinations behandling med doxorubicin og olaratumab, hvorfor olaratumab blev trukket tilbage.
Referencer	Alle nye studier er nu inkluderet i den opdaterede referenceliste.
Litteratursøgning	Der er foretaget en opdateret litteratur gennemgang indenfor alle anvende behandlingsopråder og nye studier er inkluderet i evidensstaberne. Der er ligeledes foretaget en litteratur gennemgang af immunterapi, således at dette nu også er inkluderet i retningslinjen.
Litteraturgennemgang	Gennemgange af immunterapi her helt nu og der er inkluderet et helt afsnit vedr. dette. På basis af en opgørelse vedr. dacabazin er der nu inkluderet flere studier vedr. effekten af denne behandling enten som monoterapi eller i kombination med andre former for kemoterapi.

Formulering af anbefalinger	Dacabazin i kombination med doxorubicin er en ny anbefaling. Doxorubicin og olaratumab kombinations behandling er ikke længere en anbefaling.
Behov for yderligere forskning	Der er inkluderet mere om den målrettet behandling baseret for genetiske forandringer. Denne del kræver yderlige forskning.
Bilag	Der er inkluderet et nyt bilag vedr. check point hæmmere. Derudover er der oprettet en opdateret søgestrategi og flow af ny inkluderet studier.

1. Anbefalinger (Quick guide)

Førstelinje-behandling

1. **Enkeltstof doxorubicin kan anvendes som førstelinje-behandling (B)**
2. **Kombinationsbehandling med doxorubicin og ifosfamid kan anvendes i særlige tilfælde, specielt ved histologiske subtyper følsomme for ifosfamid, hvor tumorregression kan være en særlig fordel og hos patienter som er i god performance status. (A)**
3. **Kombinationsbehandling med gemcitabin og docetaxel kan være alternativ førstelinje-behandling specielt ved uterint leiomyosarkom. (C)**
4. **Kombinationsbehandling med trabectedin og doxorubicin kan anvendes ved leiomyosarkom (C)**
5. **Kombinationsbehandling med doxorubicin og dacarbazin kan anvendes ved leiomyosarkom (B)**

Behandlinger efter førstelinje

6. **Ifosfamid højdosis såfremt dette ikke er anvendt i førstelinje - dog ikke ved uterint leiomyosarkom (C)**

7. **Trabectedin - specielt ved myxoidt liposarkom og leiomyosarkom (B)**
8. **Docetaxel+gemcitabin såfremt dette ikke er anvendt i førstelinje eller docetaxel/gemcitabin+dacarbazin (B)**
9. **Pazopanib kan anvendes ved ikke-lipogent bløddelssarkom (B). Pazopanib kan dog overvejes anvendt ved dedifferentieret liposarkom (C)**
10. **Eribulin kan anvendes ved liposarkom (B)**
11. **Regorafenib kan anvendes ved ikke-lipogent bløddelssarkom (C)**
12. **Dacarbazin monoterapi kan anvendes (afhængigt af styrke) til patienter med leiomyosarkom, såfremt det ikke er givet som førstelinje-behandling (B)**
13. **Check-point hæmmere til patienter med udifferentieret pleomorft sarkom, alveolar soft part sarkom, angiosarkom. Herudover kan check-point hæmmere evt. anvendes ved sjældne typer af sarkomer, hvor case-studier har vist en behandlingseffekt (C).**
14. **Generelt skal patienter, der er progredieret på antracyclinbaseret kemoterapi, indgå i kliniske forsøg, såfremt disse er tilgængelige for inklusion. Dette gælder også forsøg som er baseret på genetiske forandringer (C).**

Pallierende behandling af specifikke histologiske subtyper

Angiosarkom

15. **Angiosarkom kan behandles med taxaner eksempelvis docetaxel eller ugentlig paclitaxel (B). Gemcitabin enkelstof evt. i kombination med docetaxel (C). Caelyx samt pazopanib kan ligeledes anvendes på indikationen (C)**

2. Introduktion

Bløddelssarkomer er en heterogen gruppe af tumorer udgående fra kroppens bindevæv. Der findes mere end 50 forskellige histologiske undergrupper(1). Patienter i alle aldersgrupper diagnosticeres med bløddelssarkom. Bløddelssarkomer er sjældne tumorer med en estimeret incidens på 4-5/100.000 om året i Europa. I Danmark diagnosticeres ca. 250 nye tilfælde om året(2, 3). Den 5-års sygdomsspecifikke overlevelse er omkring 75% for patienter med lokaliseret sygdom. På diagnosetidspunktet har ca. 12% af patienterne metastatisk sygdom(4), patienter med dissemineret sygdom har en yderst dårlig prognose(5).

Formål

Det overordnede formål med retningslinjen er at understøtte en evidensbaseret kræftindsats af høj og ensartet kvalitet på tværs af Danmark. Da sarkomer udgør en sjælden og heterogen sygdomsgruppe, er nationalt og internationalt samarbejde afgørende i forhold til udarbejdelse af kliniske retningslinjer for behandling og udvikling af kliniske studier.

Patientgruppe

Retningslinjen dækker patienter med bløddelssarkom, hvor kurativ intenderet behandling ikke er mulig. Retningslinjen dækker kun voksne sarkompatienter, dvs. patienter over 18 år, og den inkluderer ikke patienter med Kaposi sarkom, solitære fibrøse tumorer, uterint endometrielt stromalt sarkom (ESS), udifferentieret endometrielt sarkom (UES), Gastro Intestinal Stromal Tumor (GIST), ekstraskelletalt Ewings sarkom, Ewing-lignende sarkomer samt embryonale/alveolære rhabdomyosarkomer.

Målgruppe for brug af retningslinjen

Denne retningslinje skal primært understøtte det kliniske arbejde og udviklingen af den kliniske kvalitet, hvorfor den primære målgruppe er klinisk arbejdende sundhedsprofessionelle i det danske sundhedsvæsen. Retningslinjen er vejledende og må aldrig træde i stedet for en individualiseret lægelig vurdering. Da behandlingen af sarkomer er centraliseret til 2 nationale centre, er denne retningslinje primært udarbejdet til sundhedspersonale (læger og sygeplejersker) på de to centre.

3. Grundlag

Førstelinje-behandling

1. **Enkeltstof doxorubicin kan anvendes som førstelinje-behandling (B)**
2. **Kombinationsbehandling med doxorubicin og ifosfamid kan anvendes i særlige tilfælde, specielt ved histologiske subtyper følsomme for ifosfamid, hvor tumorregression kan være en særlig fordel og hos patienter som er i god performance status. (A)**
3. **Kombinationsbehandling med gemcitabin og docetaxel kan være alternativ førstelinje-behandling specielt ved uterint leiomyosarkom. (C)**
4. **Kombinationsbehandling med trabectedin og doxorubicin kan anvendes ved leiomyosarkom (C)**
5. **Kombinationsbehandling med doxorubicin og dacarbazin kan anvendes ved leiomyosarkom (B)**

Litteratur og evidensgennemgang

39 original-studier (se evidensstabel - doxorubicin) og 2 review-artikler (se evidensstabel – review) danner grundlaget for følgende anbefalinger.

Ved metastatisk sygdom er kemoterapeutiske regimer baseret på antracykliner som førstelinje-behandling(6, 7) (1b, 1a).

Kombinationsbehandling med doxorubicin plus ifosfamid er ikke bedre end doxorubicin monoterapi, når det gælder overlevelse(5, 7-9) (1b, 1a, 1b, 1b). 3-stof kombination doxorubicin plus ifosfamid og dakarbazin er vist at give højere responsrater i forhold til 2-stof behandling med doxorubicin plus ifosfamid. 3-stof behandlingen er dog aldrig undersøgt i forhold til doxorubicin alene. Kombinationsbehandlingerne giver mere toksicitet end enkeltstof behandling med doxorubicin(10) (1b).

Median overlevelse ved enkeltstof doxorubicin øges fra ca. 8 til 19 måneder, med objektive responsrater (ORR) på mellem 9% og 24% og Progressions Fri Overlevelse (PFS) på mellem 2.7 og 6.4 måneder (5, 8, 9, 11-18) (1b, 1b, 1b, 1b, 1b, 2b, 1b, 2b, 2b, 1b, 1b). Doxorubicin enkeltstof kan give Disease Control Rate (DCR) på op til 68%(15) (2b).

Et randomiseret fase 3 studie har undersøgt doxorubicin vs ifosfamid som førstelinje-behandling med bedste responsrater for doxorubicin (12) (1b). Doxorubicin vs epirubicin som første linje behandling er ligeledes undersøgt. Man fandt ingen forskel i PFS eller overlevelse, men der var et toksisk dødsfald (cardiotoksicitet) i epirubicin-gruppen (11) (1b).

Olaratumab er et humant monoklonalt platelet-derived growth factor (PDGF) antistof, hvis godkendelse bygger på et randomiseret fase 2 studie, som viste en overlevelsesfordel på 11.8 måneder for olaratumab plus doxorubicin i forhold til doxorubicin alene (16) (2b). Et senere fase 3 studie viste dog ingen effekt af doxorubicin i kombination med olaratumab i forhold til doxorubicin monoterapi, hvorfor denne kombination ikke anbefales(19) (1b).

Kombinationsbehandling med gemcitabin og docetaxel versus enkeltstof doxorubicin som førstelinje-behandling er undersøgt i et randomiseret fase 3 forsøg. Studiet fandt ingen signifikant forskel i PFS eller overlevelse, dog tendens til lidt bedre OS på 17.8 måneder for patienter behandlet med doxorubicin mod 15.7 måneder for patienter behandlet med gemcitabin plus docetaxel. Der var ingen signifikant forskel i graden af toksicitet eller livskvalitet(17) (1b). Gemcitabin plus docetaxel kan således være en alternativ førstelinje-behandling (1b).

Et randomiseret forsøg med doxorubicin vs docetaxel som førstelinje-behandling blev lukket før tid, da ingen patienter responderede på docetaxel (20) (2b).

Et randomiseret forsøg har sammenlignet doxorubicin med trabectedin og ikke fundet forskel i PFS, studiet blev lukket og rapporterede ikke overlevelsedata (21) (2b). I translokerede sarkomer har doxorubicin vist højere ORR i forhold til trabectedin som førstelinje-behandling (22) (a). Kombinationsbehandling med doxorubicin og trabectedin medfører ikke en øget PFS ved dissemineret bløddelssarkom i forhold til doxorubicin monoterapi (23) (2b). Kombinationsbehandling med trabectedin og doxorubicin er undersøgt i leiomyosarkom med høje ORR på op til 59.6% og DCR på 87.3% for uterint leiomyosarkom mens ORR og DCR var henholdsvis 39.4% og 91.8% for ikke-uterint leiomyosarkom. PFS for uterint leiomyosarkom var 8.2 måneder og for ikke-uterint leiomyosarkom 12.9 måneder. 109 patienter indgik i dette single-arm studie (24) (2b).

Ifosfamid + epirubicin som førstelinje-behandling har vist ORR på 48-52% , PFS mellem 6.3 og 8.5 måneder og på OS 9.3 til 24 måneder (25-30) (2b, 2c, 2b, 2b, 2b, 2b). Se evidens tabel (ifosfamid). Fælles for alle disse studier er, at der er få patienter og der er ingen randomisering, hvorfor evidensniveauet for denne behandling er lav.

Et retrospektivt studie inkluderende 303 patienter med leiomyosarkom viste en signifikant øget PSF på 9.2 måneder ved kombinationsbehandling med doxorubicin og dacarbazin i forhold til doxorubicin monoterapi, som gav en PFS på 4.8 måneder. Der var ligeledes en signifikant øget overlevelse på 36.6 måneder ved kombinationsbehandling i forhold til doxorubicin monoterapi, som gav en overlevelse på 30.2 måneder (31) (2b).

Patientværdier og – præferencer

Valg af behandling afhænger i høj grad af patientens performance status og komorbiditet, da behandlingen kan medføre betydelig toksicitet herunder bl.a. myelosuppression og cardiotoksicitet.

Rationale

Rationalet bag udformningen af retningslinjen er ønske om at følge internationale guidelines.

Bemærkninger og overvejelser

De anførte regimer er allerede veletableret standard i pallierende behandling af bløddelssarkom i Danmark. Der er således ingen logistiske udfordringer i at efterleve anbefalingerne.

Behandlinger efter førstelinje

6. **Ifosfamid højdosis såfremt dette ikke er anvendt i førstelinje - dog ikke ved uterint leiomyosarkom (C)**
7. **Trabectedin - specielt ved myxoidt liposarkom og leiomyosarkom (B)**
8. **Docetaxel+gemcitabin såfremt dette ikke er anvendt i førstelinje eller docetaxel/gemcitabin+dacarbazin (B)**
9. **Pazopanib kan anvendes ved ikke-lipogent bløddelssarkom (B). Pazopanib kan dog overvejes anvendt ved dedifferentieret liposarkom (C).**
10. **Eribulin kan anvendes ved liposarkom (B)**
11. **Regorafenib kan anvendes ved ikke-lipogent bløddelssarkom (C)**
12. **Dacabazin monoterapi kan anvendes til patienter med leiomyosarkom, hvis dette ikke er givet som førstelinje behandling (B)**
13. **Check-point hæmmere kan anvendes til patienter med udifferentieret pleomorft sarkom, alveolar soft part sarkom og angiosarkom. Herudover kan check-point hæmmere evt. anvendes ved sjældne typer af sarkomer, hvor case-studier har vist en behandlingseffekt (C).**
14. **Generelt skal patienter, der er progredieret på antracyklinbaseret kemoterapi, indgå i kliniske forsøg, såfremt disse er tilgængelige for inklusion. Dette gælder også forsøg som er baseret på genetiske forandringer (C).**

Litteratur og evidensgennemgang

Ifosfamid højdosis (evidens B)

Se evidensstabel – ifosfamid som inkluderer 24 studier samt 1 review (se evidensstabel – review). Disse studier danner grundlaget for anbefalingen.

Flere single-arm, fase 2 studier har vist, at højdosis ifosfamid kan have en effekt ved forskellige histologiske undertyper af bløddelssarkom (32-37) (2c,2c, 2c, 2b, 1a, 2c), Samme studier har vist, at leiomyosarkomer har lave objektive responsrater på <10% på denne behandling. Generelt varierer ORR ved ifosfamid monoterapi fra 16% til 39% og median PFS varierer mellem 3.5-8 måneder. I disse studier er ifosfamid anvendt efter anthracyclinbaseret kemoterapi.

Trabectedin (evidens B)

I forbindelse med udarbejdelsen af denne retningslinje er der identificeret 25 studier, der danner grundlag for anbefalingerne vedr. trabectedin (se evidensstabel – trabectedin).

Flere single-arm fase 2 undersøgelser har vist, at trabectedin har effekt på forskellige histologiske subtyper af bløddelssarkom. ORR svinger fra 5% til 26.6%, mens de samme studier har vist en median PFS mellem 1.6 og 5.9 måneder (38-47) (2b). For leiomyosarkom har man fundet en median PFS på op til 5.8 mdr. i et enkelt studie (48) (2b).

Et randomiseret fase 2 forsøg har undersøgt trabectedin mod best supportive care i translokerede sarkomer og fundet at trabectedin som 2. linjebehandling er bedre med en median PFS på 5.6 måneder versus 0.9 måneder for best supportive care (49) (2b). Et andet randomiseret fase 3 studie af Le Cesne bekræftede dette med en PFS på 3.1 måneder ved trabectedin behandling mod 1.5 måned ved best supportive care (50) (1b). To randomiserede studier har sammenholdt trabectedin vs dacarbazin som 2.-linjebehandling til liposarkom og/eller leiomyosarkom. Begge studier fandt bedre PFS ved trabectedin (51, 52) (a, 2a). Et senere randomiseret fase 3 studie inkluderende 577 patienter viste, at der ikke var forskel i overlevelsen mellem de patienter, der havde modtaget trabectedin, versus de patienter, der havde modtaget dacarbazin (53) (1b). Høje responsrater er set ved specielt myxoidt liposarkom (54) (2b) og leiomyosarkomer. Bivirkninger til behandlingen er forbigående transaminasestigning og moderat myelosuppression.

Gemcitabin monoterapi eller kombinationsbehandling involverende docetaxel, gemcitabin eller dacarbazin (evidens B)

Se evidensstabel - gemcitabin, som inkluderer 17 studier, der danner grundlag for anbefalingen.

I et af de første studier, der undersøgte effekten af gemcitabin enkeltstof, var der inkluderet 17 gastro-intestinale leiomyosarkomer, og ingen af disse responderede på gemcitabin. ORR for den resterende del af populationen var på 18%, mens median PFS var 3 måneder (55) (2b). Andre studier, som har undersøgt gemcitabin enkeltstof til bløddelssarkomer, har fundet lidt lavere såvel PFS som objektive responsrater (56-58) (1b, 1b, 1b). Af de studier der har undersøgt effekten af enkeltstof gemcitabin er respondere ofte fundet blandt subtypen angiosarkom (59) (2b).

Kombinationsbehandling med gemcitabin og docetaxel har vist sig mere effektiv end gemcitabin enkeltstof i flere histologiske undergrupper, kombinationsbehandlingen er dog mere toksisk. Et studie har vist at ORR for enkeltstof gemcitabin var 8% og for kombinationsbehandling 18 %, PFS for gemcitabin enkeltstof var 3

måneder og PFS for kombinationsbehandling var 6.2 måneder (60) (2b). I en retrospektiv opgørelse af kombinationsbehandling gemcitabin og docetaxel fandt man, at behandlingen var mere effektiv ved leiomyosarkomer i forhold til andre histologiske undertyper (61) (1b). Gemcitabin kombineret med dacarbazin har ligeledes vist sig mere effektiv end dacarbazin enkeltstof med en PFS på op til 9.25 måneder for kombinationsbehandlingen (62, 63) (2b, 2b). Gemcitabin plus vinorelbin i kombination er ligeledes undersøgt med PFS på 3.4 måneder hos patienter med avanceret bløddelssarkom (64) (1b). Kombinationsbehandlingen gemcitabin og docetaxel/dacarbazin er mere effektiv end gemcitabin alene (B).

Dacarbazin (evidens B)

Se evidensstabel – (doxorubicin, trabectedin, gemcitabin og kemoterapi andet).

Flere studier har undersøgt dacarbazin enkeltstof enten som single arm studie eller mod en kombinationsbehandling hvor dacarbazin indgår. Generelt er ORR for dacarbazin monoterapi 3-18% afhængig af den histologiske subtype (65, 66) (2b,1b). Den mediane PFS varierede mellem 1.5 og 4.2 mdr (51, 52, 66) (a,1b,1b), OS mellem 8 og 13.1 måneder afhængig af den histologiske subtype. Dacarbazin er traditionelt anvendt i kombination med andre stoffer, specielt i kombination med doxorubicin i forskellige regimer hvor effekten er større end ved monoterapi. Se de enkelte afsnit (6, 67) (1b,1b).

Pazopanib (evidens C)

Se evidensstabel - targeteret behandling, hvor 9 studier indgår i udarbejdelsen af anbefalingen.

Pazopanib er en multitargeteret tyrosinkinasehæmmer. Grundlaget for anvendelse af pazopanib er et fase 2 studie med 142 patienter og et randomiseret fase 3 studie med 372 patienter med metastatisk ikke lipogent bløddelssarkom. Der var en signifikant bedre median progressionsfri overlevelse på 4.6 måneder mod 1.6 måneder i placebo-armen. Total overlevelse var ikke signifikant bedre i pazopanib-armen (68)(1b). Bivirkninger inkluderede blandt andet forhøjet blodtryk og påvirkede leverparametre.

Et mindre studie inkluderende 42 patienter med liposarkom, påviste en DCR på 68%, en median PFS på 4.4 måneder og en median OS på 12.6 måneder. Den største effekt blev påvist for dedifferentieret liposarkom med PFS på 6.2 måneder mod 3.2 måneder for myxoid liposarkom (69) (2b). En retrospektiv opgørelse har påvist at effekten af pazopanib hæmmes af samtidig behandling med syrepumpehæmmere (70) (4).

Eribulin (evidens B)

Se evidensstabel - targeteret behandling, hvor 5 studier danner grundlag for anbefalingerne.

Et fase 3 forsøg har sammenlignet effekten af eribulin med dacarbazin hos patienter med bløddelssarkom, som tidligere har modtaget antracyclinbaseret kemoterapi. Eribulin og dacarbazin gav samme PFS på 2.6 måneder, herudover påviste forsøget en OS på 13.5 måneder for eribulin mod 11.5 måneder for dacarbazin (71) (2b). Subgruppeanalyse viste at liposarkomer havde en DCR på 64% og en totaloverlevelse på 15.6 måneder for eribulin mod 8.4 måneder for dacarbazin (72) (2b). I et tidligere fase 2 studie som inkluderede 128 patienter med STS fandt man en DCR på 47.6 % for dedifferentieret liposarkom (73) (2b).

Regorafenib (evidens C)

Se evidensstabel - targeteret behandling, hvor et randomiseret studie og et fase 2 studie ligger til grund for anbefalingen.

Regorafenib versus placebo har i et randomiseret forsøg med 182 patienter vist en effekt ved specielt synovialt sarkom med en DCR på 77% og en PFS på 5.6 måneder mod 1.0 måned for placebo. For liposarkom var der ingen effekt, hvorimod der for leiomyosarkom var en lille gevinst på PFS på 3.7 måneder for regorafenib mod 1.8 måneder i placebo gruppen (74) (1b).

Check-point hæmmere (evidens C)

Se evidensstabel – check-point hæmmere, hvor 30 studier ligger til grund for denne anbefaling. Sarkom er en meget sjælden kræftform bestående af mange forskellige histologiske undertyper. De første studier hvor man undersøgte effekten af immunterapi inkluderede man flere forskellige histologiske undertyper(75)(2c). Der er efterhånden et stigende evidensgrundlag for at anvende check-point hæmmere ved særlige histologiske undertyper. Studier har vist at 50 - 80% af patienter med udifferentieret pleomorft sarkom, angiosarkom, alverlar soft part sarkom, eller selektive meget sjældne undertyper har effekt af behandlingen. ORR for alle sarkomer uanset undertype ligger mellem 11 og 49% (76-82) (2c, 1c, 2b, 2b, 2a, 2c, 1c), for udvalgte grupper har man fundet DCR op til 70% (83) (2b). De forskellige studier påviste en median progressionsfri overlevelse mellem 2.7 og 8.1 måneder, hvilket er bedre end standard kemoterapi (76, 81, 82, 84) (2c, 2c, 1c, 2c). Et retrospektivt studie har fundet en median PFS på 24.4 måneder blandt patienter med effekt af behandlingen (81) (2c). Enkelte studier har ligeledes beskrevet patienter med komplet respons på behandlingen(85, 86) (2c,2c). Forskellige kombinationer af kemoterapi/tyrosinkinase hæmmere og check point hæmmere er ved at blive undersøgt, og enkelte studier har vist lovende resultater (76, 78, 87-89) (2c,2b,2b,2b, 2c).

Targeterbar behandling baseret på genetiske forandringer (evidens D)

Flere studier har undersøgt forekomsten af genetiske forandringer ved sarkomer, og selv om sarkomer generelt har en lav tumor mutations bryde (TMB), findes der ofte et højt copy number alterations (CNA). I en undersøgelse fra Groisberg et al. fra 2017 fandt de, at ud af 102 sarkompatienter havde 94 (93%) mindst en genetisk fordring. De mest almindelige var *TP53*, *CDK4*, *MDM2*, *RB1*, *CDKN2A/B* og *FRS2*. Studiet viste, at 62 patienter (61%) havde et potentielt target, hvortil der findes en behandling (90) (2b). I en artikel publiceret i 2018 af Lucchesi et al. fandt man tilsvarende tal for antallet af patienter med targeterbare genetiske forandringer. Her blev 584 patienter undersøgt og 494 (85%) havde mindst en mutation. Her fandt man ligeledes, at de mest almindelige mutationer var *TP53*, *MDM2*, *CDK4*, *RB*, *ATRX*, *CDKN2A*, *PTEN* og *NF1*. For 239 patienter (41%) fandt man en mutation, hvor der potentielt er behandling (91) (2b).

Den seneste opgørelse fra Gusho et al. 2021, hvor 136 sarkompatienter blev undersøgt, viste at 122 patienter havde mindst en mutation (89,4%), og at de mest almindelige mutationer var *TP53*, *CDKN2A/B*, *RB1*, *CDKN2A*, *ATRX*, *FRS2* og *MDM2/CDK4*. 47.1% af patienterne havde en mutation, hvortil der var en behandling (92) (2b).

Den kliniske effekt af målrettet behandling hos sarkom patienter mangler at blive afklaret. Anvendelse af targeteret behandling baseret på genetiske forandringer må bero på individuel vurdering. Genetiske undersøgelser kan, såfremt det er muligt, foretages hvis der ikke er yderligere behandlingstilbud eller såfremt

det ud fra histologiske undertype findes hensigtsmæssigt. *Det kræver dog, at patienter har en almen tilstand, der tillader, at de kan indgå i off-label behandling, eller kliniske forsøg med targeterbare behandlinger.*

Patientværdier og – præferencer

Behandlingsvalg efter initial anthracyklinbaseret kemoterapi afhænger af histologisk subtype, komorbiditet, performance status samt patienthensyn.

Rationale

Rationalet bag udformningen af retningslinjen er ønske om at følge internationale guidelines.

Bemærkninger og overvejelser

Sarkomer er en heterogen gruppe af tumorer og repræsenterer en meget heterogen gruppe af patienter. Det er derfor vigtigt at tage hensyn til patientens alder, komorbiditet, almen tilstand, histologisk undertype, tidligere behandling og sygdomsudbredning samt individuelle patientønsker når behandlingsovervejelser diskuteres. Andre onkologiske behandlingsmodaliteter herunder blandt andet stråleterapi samt best supportive care bør naturligvis også indgå i behandlingsovervejelserne.

Ovenforstående anbefalinger bygger på en grundig litteraturgennemgang, klinisk erfaring og international konsensus. Studierne, der indgår i denne retningslinje, er ofte små eller inkluderer mange forskellige histologiske undertyper af sarkomer.

Pallierende behandling af specifikke histologiske subtyper.

Angiosarkom

- 15. Angiosarkom kan behandles med taxaner eksempelvis docetaxel eller ugentlig paclitaxel (B). Gemcitabin enkelstof evt. i kombination med docetaxel (C). Caelyx samt pazopanib kan ligeledes anvendes på indikationen (C).**

Litteratur og evidensgennemgang

Angiosarkom

Caelyx versus doxorubicin (evidenstabel – doxorubicin) er blevet undersøgt i et randomiseret studie med 94 patienter. ORR for både doxorubicin og caelyx var lave i dette studie formentlig pga. et stort antal patienter med gastrointestinal stromal tumor (GIST), som udgjorde 33% af alle patienterne. Man fandt, at caelyx og doxorubicin havde samme ORR og PFS, men at caelyx var langt mindre marv- og cardiotoksisk men mere hudtoksisk (93) (2b). Caelyx ophobes i tumor og hud og har en halveringstid på op til 50 timer. Et lille case-baseret studie med 6 patienter med angiosarkom har vist effekt af caelyx (94) (3). Caelyx har vist sig effektiv ved den vaskulære tumor Kaposi sarkom, hvorfor caelyx ligeledes tænkes anvendt ved angiosarkom (95)(2c). En retrospektiv undersøgelse omfattende 125 patienter med angiosarkom fandt PFS på 4.2 måneder ved behandling med caelyx (11 patienter havde modtaget denne behandling), 4.0 måneder ved paclitaxel (41 patienter), 2.2 måneder ved enkelstof gemcitabin (11 patienter) og 1.6 måneder ved ifosfamid (12

patienter)(96). En retrospektiv opgørelse har vist at enkeltstof gemcitabin har effekt ved angiosarkom med ORR på 68% og median OS på 17 måneder. 3 af disse patienter blev behandlet med kombination gemcitabin plus taxan, 2 havde partielt respons og en havde stabil sygdom (97)(3).

Angiosarkomer er følsomme for taxaner, som derfor kan anvendes som førstelinje behandling [B]. Paclitaxel (evidenstabel - kemoterapi) som enkeltstof har i single-arm studier vist en ORR på 7 til 53% med størst ORR for angiosarkom(98)(2c). Generelt er disse studier dog små. Behandling af angiosarkom med paclitaxel er vist at give en PFS på 6.6 måneder og en OS 19.5 måneder (99) (2b).

Et større randomiseret studie har undersøgt doxorubicin versus paclitaxel til behandling af angiosarkom. ORR for doxorubicin var 29% og for paclitaxel 53%, PFS for doxorubicin var 3 måneder mod 5.8 måneder for paclitaxel. OS var 10.3 måneder for paclitaxel mod 5.5 måneder for doxorubicin (100) (2b). Paclitaxel er forsøgt kombineret med bevacizumab ved angiosarkom i et randomiseret fase 2 studie. Kombinationsbehandlingen havde samme PFS som paclitaxel alene 6.6 måneder (99) (2b).

Pazopanib anvendt ved vaskulære sarkomer har vist ORR på 23 %, DCR på 54 %, PFS på 3 måneder og OS på ca. 10 måneder (101) (3).

Patientværdier og – præferencer

Valget af behandling bygger primært på klinisk erfaring, patientperformance samt komorbiditet.

Rationale

Rationalet bag udformningen af retningslinjen er et ønske om at følge internationale guidelines.

Bemærkninger og overvejelser

Angiosarkom er en sjælden subtype af bløddelssarkom. Anbefalingerne i denne retningslinje bygger på små studier og retrospektive opgørelser.

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5. Metode

Litteratursøgning

Foreliggende litteratur er tilvejebragt på basis af grundig litteraturgennemgang (se søgeprotokol – bilag 1, søgeprotokol bilag 1 version 2, søgeprotokol bilag 1b). Der er primært taget udgangspunkt i originallitteratur, hvorudfra der er foretaget en grov selektion med frasortering af ikke relevante publikationer (se bilag 2). Evidenstabeller (bilag 3 – 10, og 12) er efterfølgende udfærdiget, evidensniveauet er anført. Retningslinjerne er herefter udarbejdet og efterfølgende justeret/suppleret med informationer fra internationale guidelines (se søgeprotokol – bilag 1, søgeprotokol bilag 1 version 2). Reviewartikler er anvendt i begrænset omfang for at sikre, at relevant litteratur er inkluderet (se flowchart - bilag 2, flowchart bilag 2 version 2). Metaanalyser er anvendt i det omfang de har været tilgængelige og relevante. Hvor der ikke har været evidens bygger anbefalingerne på ekspertkonsensus.

Litteraturgennemgang

Litteraturgennemgang er foretaget af Ninna Aggerholm Pedersen. Det er primært originallitteratur med specifikt fokus på kliniske forsøg, der danner grundlaget for denne retningslinje.

Formulering af anbefalinger

Anbefalingerne er formuleret af Ninna Aggerholm Pedersen og Philip Blach Rossen. Anbefalingerne forelægges og diskuteres ved årsmøde i DSG primo januar 2019. Denne er efterfølgende revideret. Den revideret er fremlagt og diskuteret på DSG årsmøde januar 2022

Interessentinvolvering

Der har ikke været patienter eller andre ikke-DSG medlemmer involveret i udarbejdelsen af denne retningslinje.

Høring og godkendelse

Retningslinjen er sendt til høring blandt DSG's medlemmer forud for DSG's årsmøde primo januar 2019. Den reviderede udgave er sendt til høring december 2021. Retningslinjen for pallierende medicinsk behandling af patienter med bløddelssarkom er forelagt og diskuteret ved DSG's årsmøde januar 2022 og efterfølgende godkendt af DSG's medlemmer og bestyrelse.

Anbefalinger, der udløser betydelig merudgift

De i retningslinjen direkte anførte behandlingsanbefalinger vil ikke medføre betydelige merudgifter, da de i væsentligt omfang allerede er implementerede på de 2 nationale sarkomcentre. Behandling med immunterapi anvendes i dag off-label på AUH og som standard behandling på Herlev. Der er søgt om tilladelse til at anvende immunterapi som standard behandling på AUH. Da behandlingen gives off-label vil det således ikke betyde en merudgift.

Nationalt samt internationalt samarbejde med fokus på at forbedre behandlingsmuligheder for sarkompatienter aktuelt samt fremadrettet er væsentligt. Fokus på og styrkelse af internationalt klinisk samt forskningsmæssigt samarbejde er essentielt og bør prioriteres højt. Løbende udvikling og forbedring af eksisterende behandlingstilbud til sarkompatienter er væsentlig. Anbefalingen omkring deltagelse i kliniske forsøg kan medføre merudgifter. Deltagelse i kliniske forsøg, nationalt og internationalt, medfører merudgifter til GCP-monitorering, KFE støtte, juridisk bistand, medarbejderfrikøb mhp. varetagelse af protokolansvar mm.

Behov for yderligere forskning

Der er i høj grad behov for yderligere forskning inden for behandling herunder pallierende behandling af sarkompatienter. Prognosen for disse patienter er dårlig, og evidensen for mange at de behandlinger der tilbydes, bygger på små ikke-randomiserede studier. Sarkomer er, som tidligere anført, en sjælden og heterogen sygdom, med de forsknings- og behandlingsmæssige implikationer det medfører. Der er derfor behov for yderligere forskning indenfor området samt udvikling af nye behandlingsstrategier og optimere brugen af allerede eksisterende behandling. Dette kræver en høj grad af nationalt og internationalt samarbejde også vedrørende kliniske forsøg – et samarbejde der bør fremmes såvel internationalt som ved de 2 nationale sarkomcentre.

Forfattere

- Ninna Aggerholm Pedersen, klinisk onkolog, afdelingslæge, Kræftafdelingen, Aarhus Universitetshospital
 - Philip Blach Rossen, klinisk onkolog, overlæge, Kræftafdelingen, Aarhus Universitetshospital
- Ovenstående har ingen interessekonflikter.

Version af retningslinjeskabelon

Retningslinjen er udarbejdet i version 9.2 af skabelonen.

6. Monitoreringsplan

Standarder og indikatorer

Da sarkomer er en sjælden og meget heterogen sygdomsgruppe omfattende mange forskellige histologiske subgrupper, vil behandlingen ofte bygge på en individualiseret behandlingsstrategi. Det er således ikke meningsfyldt at udvælge og monitorere på specifikke standarder og indikatorer i forbindelse med den palliative behandling af sarkom patienter.

Plan for audit og feedback

Retningslinjen skal med passende intervaller opdateres ud fra nationale og internationale peer review publicerede data.

7. Bilag

Bilag 1 – Søgestrategier

Søgestrategi (oprindelig søgestrategi)

Titel (på retningslinje)	<i>Pallierende kemoterapi til patienter med bløddelsarskom</i>
DMCG	DSG
Kontakt med metodespecialist	Nej
Senest udfyldt	22/12/2018

Afgrænsning af emne	
Baggrund	<i>Pallierende kemoterapi til patienter med bløddelssarkom</i>
Inklusions- og eksklusionskriterier	<i>Publikationsdato (periode): 1990 – 2008</i> <i>Sprog: Engelsk, dansk, svensk</i> <i>Publikationstyper: Guidelines, reviews, originale artikler</i>

Emneord	Populationen	Intervention	Sammenligningsintervention	Outcomes
Dansk	<i>Sarkom, bløddelssarkom, kræft i bløddele, kræft i bindevæv</i>	<i>Kemoterapi, targeteret behandling</i>	<i>Fase 1, 2 og 3 forsøg, kliniske forsøg</i>	<i>Effekt af behandlingen, overlevelsen, tid til progression.</i>
Engelsk	<i>Sarcoma, soft tissue sarcoma,</i>	<i>Chemotherapy, targeted treatment,</i>	<i>Clinical trials, phase I, II or III studies</i>	<i>Effect, overall survival, time to progression</i>

Søgning efter guidelines

Databaser (Guidelines)	Dato for søgning	Ansvarlig for søgningen
G-I-N International http://www.g-in.net/library/international-guidelines-library	(19/11/2018)	NAP (16 hits 4 udvalgt – 2 findes ved andre links)
NICE (UK) https://www.nice.org.uk/guidance/published?type=apg,csq,cg,mpg,ph,sq,sc	(19/11/2018)	NAP (1 guideline)
Scottish Intercollegiate Guidelines Network (SIGN) http://www.sign.ac.uk/our-guidelines.html	(19/11/2018)	NAP (ingen)
Helsedirektoratet (Norge) https://helsedirektoratet.no/retningslinjer	(19/11/2018)	NAP (1 guideline)
Socialstyrelsen (Sverige) http://socialstyrelsen.se/	(19/11/2018)	NAP (1 guideline)
Australian Clinical Practice Guidelines https://clinicalguidelines.gov.au/	(19/11/2018)	NAP (1 guideline)
European Society for Medical Oncology http://www.esmo.org/Guidelines	(19/11/2018)	NAP (1 guideline)
National Comprehensive Cancer Network https://www.nccn.org/professionals/physician_gls/default.aspx	(19/11/2018)	NAP (1 guideline)

Søgning efter systematiske reviews

Databaser (systematiske reviews)	Dato for søgning	Ansvarlig for søgningen
Medline	(13/11/2018)	NAP
The Cochrane Library	(19/11/2018)	NAP

Søgning efter primærlitteratur (fx randomiserede kontrollerede forsøg)

Databaser (primær litteratur)	Dato for søgning (dd/mm/åååå)	Ansvarlig for søgningen (navn(e))
Medline	(28/10/2018)	NAP

Søgestrategier

Guidelines søgning. Søgningen på de forskellige guidelines blev foretaget den 19.11.2018. Følgende søgeord anvendt: Sarkom; Sarcoma; kemoterapi, cytoterapi, Chemotherapy.

Medline: søgestreng anvendt til at finde review artikler. Søgning foretaget 13.11.2018.

"Sarcoma"[Mesh] AND (advanced[All Fields] AND ("drug therapy"[Subheading] OR ("drug"[All Fields] AND "therapy"[All Fields]) OR "drug therapy"[All Fields] OR "chemotherapy"[All Fields] OR "drug therapy"[MeSH Terms] OR ("drug"[All Fields] AND "therapy"[All Fields]) OR "chemotherapy"[All Fields])) AND "humans"[MeSH Terms] AND English[lang] AND Review[ptyp] AND (Review[ptyp] AND ("1990/01/01"[PDAT] : "2018/12/31"[PDAT]) AND "adult"[MeSH Terms]) NOT Kaposi's[All Fields]

Medline: søgestreng anvendt til at finde original litteratur. Søgningen foretaget 28.10.2018.

"Sarcoma"[Mesh] AND (advanced[All Fields] AND ("drug therapy"[Subheading] OR ("drug"[All Fields] AND "therapy"[All Fields]) OR "drug therapy"[All Fields] OR "chemotherapy"[All Fields] OR "drug therapy"[MeSH Terms] OR ("drug"[All Fields] AND "therapy"[All Fields]) OR "chemotherapy"[All Fields])) AND (Clinical Trial[ptyp] AND "humans"[MeSH Terms] AND English[lang])

Cochrane Library Reviews. Søgningen foretaget den 19.11.2018. Søgeord "Sarcoma and chemotherapy"

Søgestrategi for revision

Emne

Udfyld ét arbejdsblad for hvert emne.

Titel (på retningslinje)	<i>Pallierende kemoterapi og targeteret behandling til patienter med bløddelsarkom</i>
DMCG	DSG
Kontakt med metodespecialist	Nej
Senest udfyldt	15/10/2021

Afgrensning af emne	
Baggrund	<i>Pallierende kemoterapi og targeteret behandling til patienter med bløddelssarkom</i>
Inklusions- og eksklusionskriterier	<p><i>Publikationsdato (periode): 1990 – 2018 til version 1, 2018 til 2021 til version 2</i></p> <p><i>Sprog: Engelsk, dansk, svensk</i></p> <p><i>Publikationstyper: Guidelines, reviews,, originale artikler</i></p>

Emneord	Populationen	Intervention	Sammenligningsintervention	Outcomes
Dansk <i>Alle tænkelige søgeord bør indsættes.</i>	<i>Sarkom, bløddelssarkom, kræft i bløddele, kræft i bindevæv</i>	<i>Kemoterapi, targeteret behandling</i>	<i>Fase 1, 2 og 3 forsøg, kliniske forsøg</i>	<i>Effekt af behandlingen, overlevelsen, tid til progression.</i>
Engelsk <i>Alle tænkelige søgeord bør indsættes.</i>	<i>Sarcoma, soft tissue sarcoma,</i>	<i>Chemotherapy, targeted treatment,</i>	<i>Clinical trials, phase I, II or III studies</i>	<i>Effect, overall survival, time to progression</i>

Søgning efter guidelines

Databaser (Guidelines)	Dato for søgning	Ansvarlig for søgningen
G-I-N International http://www.g-in.net/library/international-guidelines-library	(19/11/2018)	NAP (16 hits 4 udvalgt – 2 findes ved andre links)
NICE (UK) https://www.nice.org.uk/guidance/published?type=apg.csg.cg.mpg.ph.sg.sc	(19/11/2018)	NAP (1 guideline)
Scottish Intercollegiate Guidelines Network (SIGN) http://www.sign.ac.uk/our-guidelines.html	(19/11/2018)	NAP (ingen)
Helsedirektoratet (Norge) https://helsedirektoratet.no/retningslinjer	(19/11/2018)	NAP (1 guideline)
Socialstyrelsen (Sverige) http://socialstyrelsen.se/	(19/11/2018)	NAP (1 guideline)
Australian Clinical Practice Guidelines https://clinicalguidelines.gov.au/	(19/11/2018)	NAP (1 guideline)
European Society for Medical Oncology http://www.esmo.org/Guidelines	(19/11/2018)	NAP (1 guideline)
National Comprehensive Cancer Network https://www.nccn.org/professionals/physician_gls/default.aspx	(19/11/2018)	NAP (1 guideline)

Søgning efter systematiske reviews

Databaser (systematiske reviews)

Dato for søgning
(13/11/2018)

Ansvarlig for søgningen

Medline

Ver. 1.0

NAP

(xx/10/2021)

Ver. 2.0

	(19/11/2018)	
	Ver 1.0	
The Cochrane Library		NAP
	(xx/10/2021)	
	Ver 2.0	

Søgning efter primærlitteratur (fx randomiserede kontrollerede forsøg)

Databaser (primær litteratur)	Dato for søgning (dd/mm/åååå)	Ansvarlig for søgningen (navn(e))
	(28/10/2018)	
	Ver. 1.0	
Medline		NAP
	(25/10/2021)	
	Ver. 2.0	

Søgestrategier

Søgning i forbindelse med version 1.0 af retningslinjen.

Guidelines søgning. Søgningen på de forskellige guidelines blev foretaget den 19.11.2018. Følgende søgeord anvendt: Sarkom; Sarcoma; kemoterapi, cytoterapi, Chemotherapy.

Medline: søgestreng anvendt til at finde review artikler. Søgning foretaget 13.11.2018.

"Sarcoma"[Mesh] AND (advanced[All Fields] AND ("drug therapy"[Subheading] OR ("drug"[All Fields] AND "therapy"[All Fields]) OR "drug therapy"[All Fields] OR "chemotherapy"[All Fields] OR "drug therapy"[MeSH Terms] OR ("drug"[All Fields] AND "therapy"[All Fields]) OR "chemotherapy"[All Fields])) AND "humans"[MeSH Terms] AND English[lang] AND Review[ptyp] AND (Review[ptyp] AND ("1990/01/01"[PDAT] : "2018/12/31"[PDAT]) AND "adult"[MeSH Terms]) NOT Kaposi's[All Fields]

Medline: søgestreng anvendt til at finde original litteratur. Søgningen foretaget 28.10.2018.

"Sarcoma"[Mesh] AND (advanced[All Fields] AND ("drug therapy"[Subheading] OR ("drug"[All Fields] AND "therapy"[All Fields]) OR "drug therapy"[All Fields] OR "chemotherapy"[All Fields] OR "drug therapy"[MeSH Terms] OR ("drug"[All Fields] AND "therapy"[All Fields]) OR "chemotherapy"[All Fields])) AND (Clinical Trial[ptyp] AND "humans"[MeSH Terms] AND English[lang])

Cochrane Library Reviews. Søgningen foretaget den 19.11.2018. Søgeord "Sarcoma and chemotherapy"

Søgning i forbindelse med version 2.0 af retningslinjen.

Samme søgestreng anvendt til at gennemgå litteraturen: søgningen blev foretaget den 25.10.2021 af NAP

Bilag 1b: Søgestrategi for immunterapi

Emne

Udfyld ét arbejdsblad for hvert emne.

Titel (på retningslinje)	<i>Pallierende kemoterapi og targeteret behandling til patienter med bløddelsarskom</i>
DMCG	DSG
Kontakt med metodespecialist	Nej
Senest udfyldt	01/11/2021

Afgrænsning af emne	
Baggrund	<i>Pallierende kemoterapi og targeteret behandling til patienter med bløddelssarkom</i>
Inklusions- og eksklusionskriterier	<i>Publikationsdato (periode): 1990 – dd</i> <i>Sprog: Engelsk, dansk, svensk</i> <i>Publikationstyper: Guidelines, Reviews, originale artikler</i>

Emneord	Populationen	Intervention	Sammenligningsintervention	Outcomes
Dansk <i>Alle tænkelige søgeord bør indsættes.</i>	<i>Sarkom, bløddelssarkom, kræft i bløddele, kræft i bindevæv</i>	<i>Pembrolizumab immunterapi</i>	<i>Fase 1, 2 og 3 forsøg, kliniske forsøg Cohorte undersøgelser, Cases</i>	<i>Effekt af behandlingen, overlevelsen, tid til progression.</i>
Engelsk <i>Alle tænkelige søgeord bør indsættes.</i>	<i>Sarcoma, soft tissue sarcoma,</i>	<i>Pembrolizumab immunotherapy</i>	<i>Clinical trials, phase I, II or III studies Cohort studies Case rapport</i>	<i>Effect, overall survival, time to progression</i>

Søgning efter guidelines

Databaser (Guidelines)	Dato for søgning	Ansvarlig for søgningen
SSG (scandinavian sarcoma group) https://www.ssg-org.net/treatment-protocols-and-recommendations/ongoing	(01/11/2021)	NAP

Søgning efter systematiske reviews

Databaser (systematiske reviews)	Dato for søgning	Ansvarlig for søgningen
Medline	20/09/2021	NAP
Embase	20/9/2021	NAP

Søgning efter primærlitteratur (fx randomiserede kontrollerede forsøg)

Databaser (primær litteratur)	Dato for søgning (dd/mm/åååå)	Ansvarlig for søgningen (navn(e))
Medline	20/9/2021	NAP
Embase	20/9/2021	NAP

Søgestrategier

Søgning i forbindelse med version 2.0 af retningslinjen, som også giver en anbefaling for anvendelse af immunterapi.

Guidelines søgning. Søgningen på de forskellige guidelines blev foretaget den 01.11.2021

Medline: søgestreng anvendt til at finde primær publikationer og review artikler. Søgning foretaget 20.09.2021.

(("pembrolizumab"[supplementary Concept] OR "pembrolizumab"[All fields]) AND ("sarcoma"[MeSH Terms] OR "sarcoma"[All Fields] OR "sarcomas"[All Fields] OR sarcoma s"[All Fields])) AND((ft[Filter]) AND (English[Filter]))

Antal publikationer 141

immunotherapy and sarcoma Filters: Full text, Clinical Trial, Meta-Analysis, Randomized Controlled Trial, Review, Systematic Review, English Sort by: Publication Date

((("immunotherapy"[MeSH Terms] OR "immunotherapy"[All Fields] OR "immunotherapies"[All Fields] OR "immunotherapy s"[All Fields]) AND ("sarcoma"[MeSH Terms] OR "sarcoma"[All Fields] OR "sarcomas"[All Fields] OR "sarcoma s"[All Fields])) AND ((clinicaltrial[Filter] OR meta-analysis[Filter] OR randomizedcontrolledtrial[Filter] OR review[Filter] OR systematicreview[Filter]) AND (ft[Filter]) AND (english[Filter]))) Translations immunotherapy: "immunotherapy"[MeSH Terms] OR "immunotherapy"[All Fields] OR "immunotherapies"[All Fields] OR "immunotherapy's"[All Fields] sarcoma: "sarcoma"[MeSH Terms] OR "sarcoma"[All Fields] OR "sarcomas"[All Fields] OR "sarcoma's"[All Fields]

Antal publikationer 718

Embase: søgestreng anvendt til at finde original litteratur og review artikler. Søgningen foretaget 13.10.2021

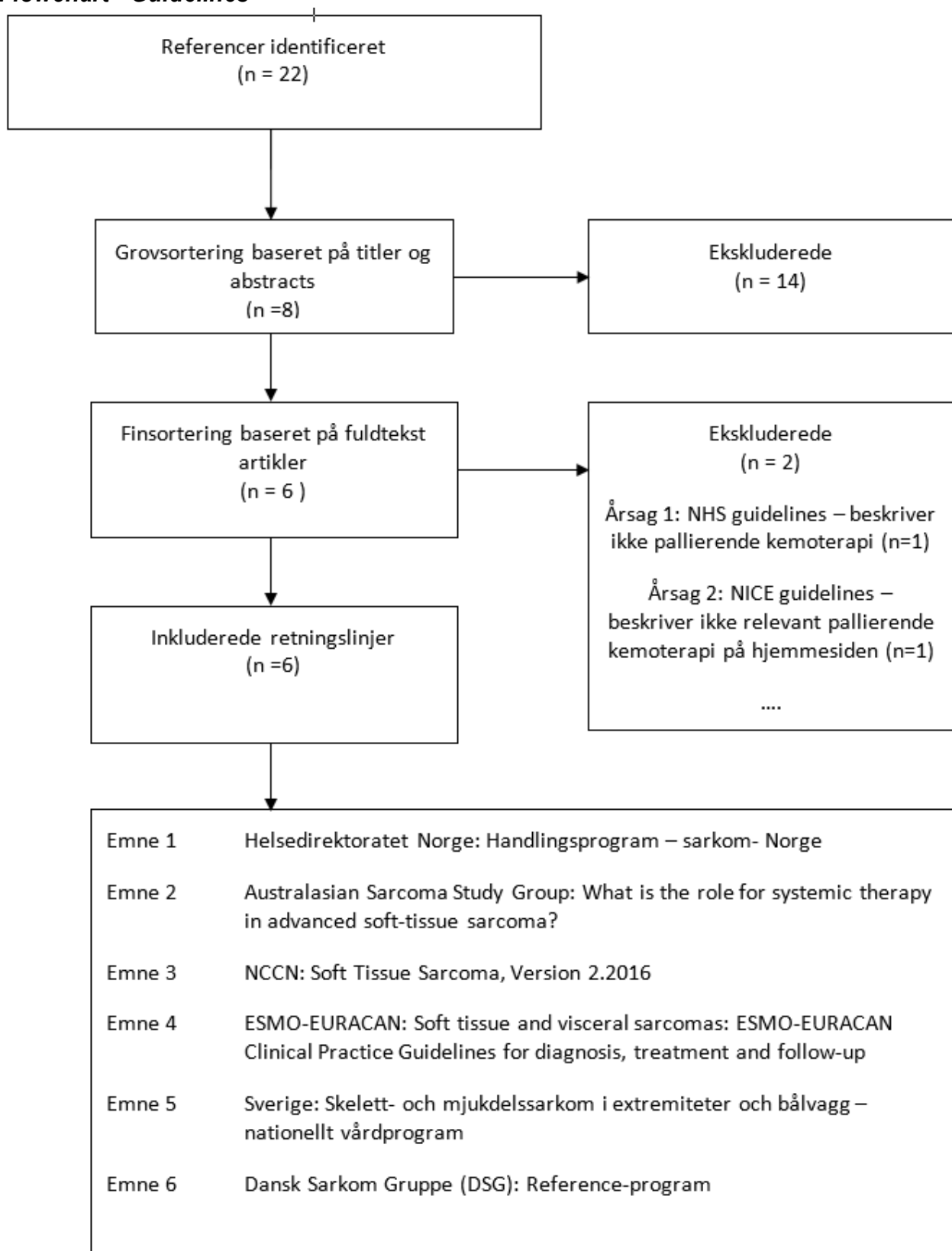
Der fremkom 698 efter fjernelse af duplikater var der 556 tilbage som blev systematiske gennemgået.

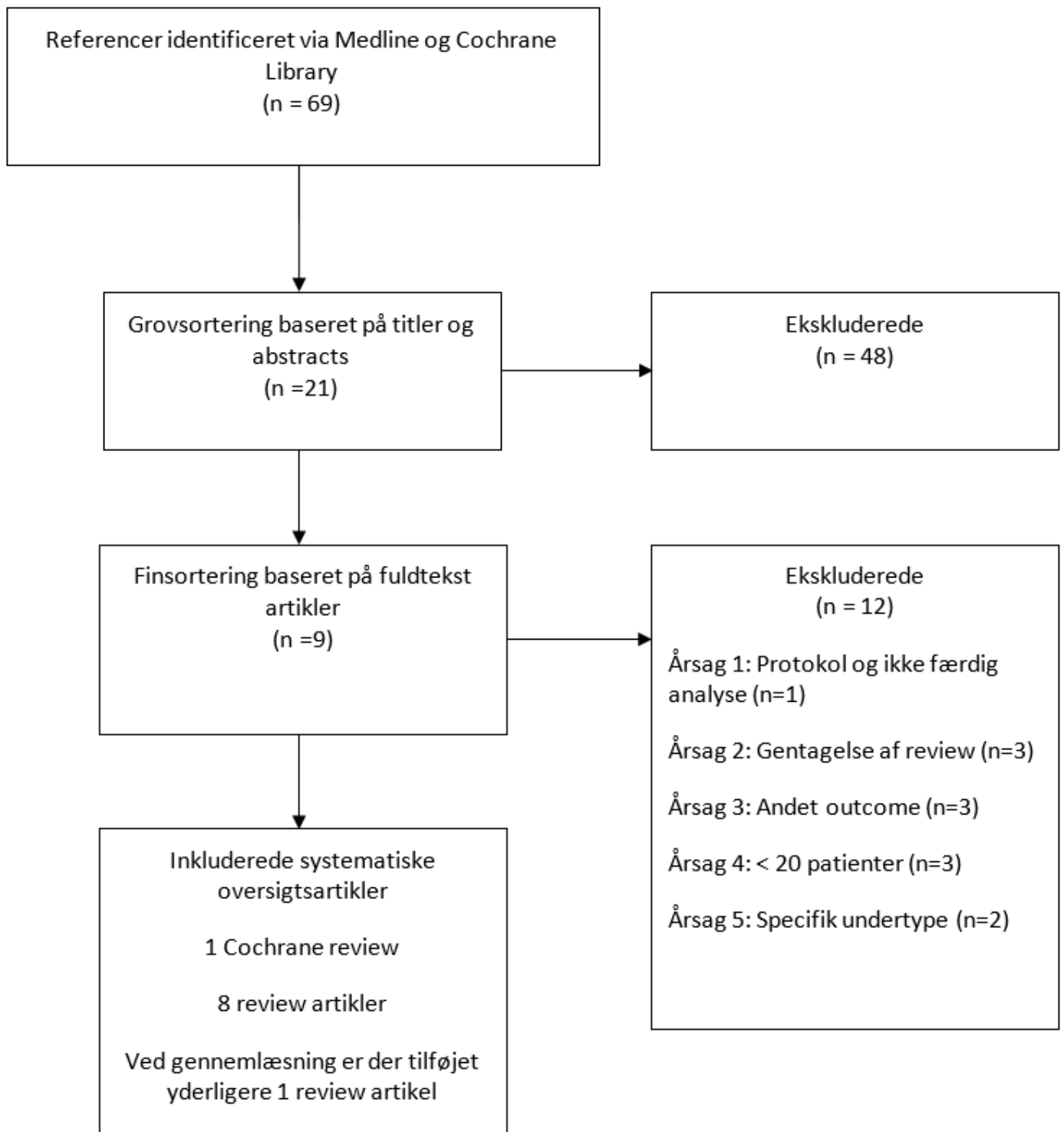
Søgestreng: ('sarcoma'/exp OR sarcoma) AND pembrolizumab AND treatment.

Yderlige 17 kliniske forsøg eller retrospektiv opgørelser blev identificeret. De fleste af disse var studie protokoller. Dette gav anledning til inklusion af yderlige 2 studier.

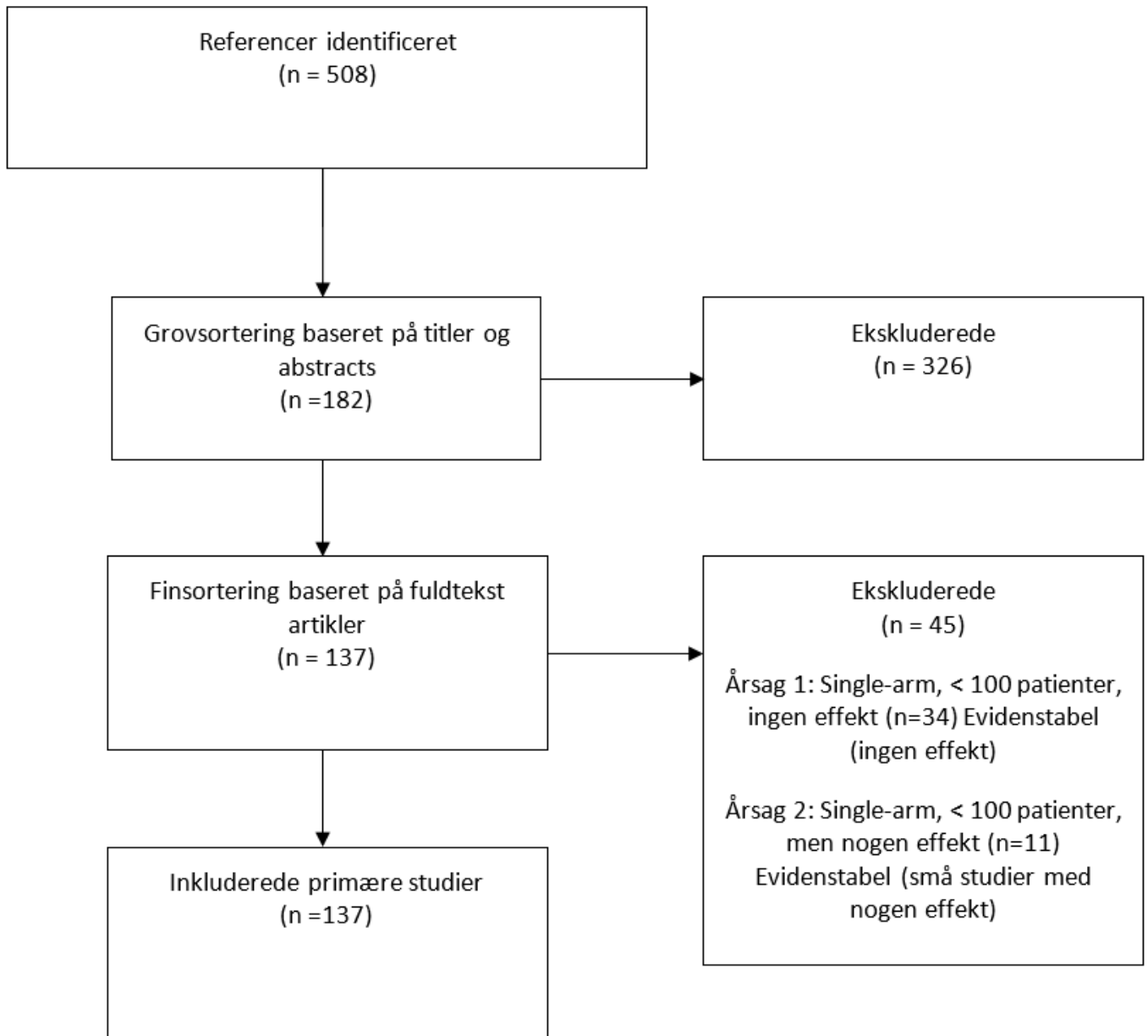
Det total antal studier inkluderet er således 30, hvoraf den ene er en pooled analyse.

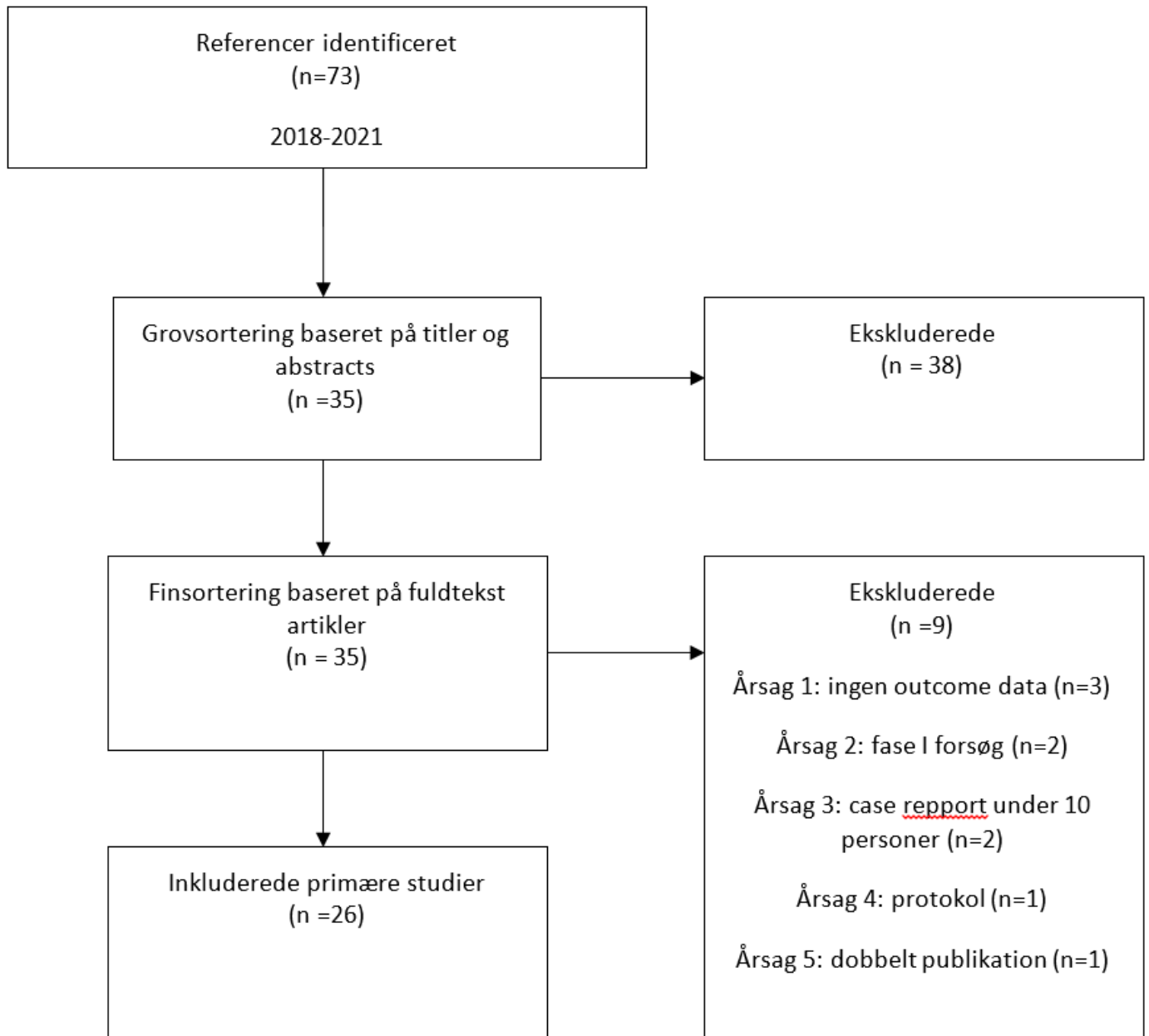
Bilag 2 – Flowchart over selekteret litteratur

Flowchart - Guidelines

Flowchart – Systematiske oversigtsartikler

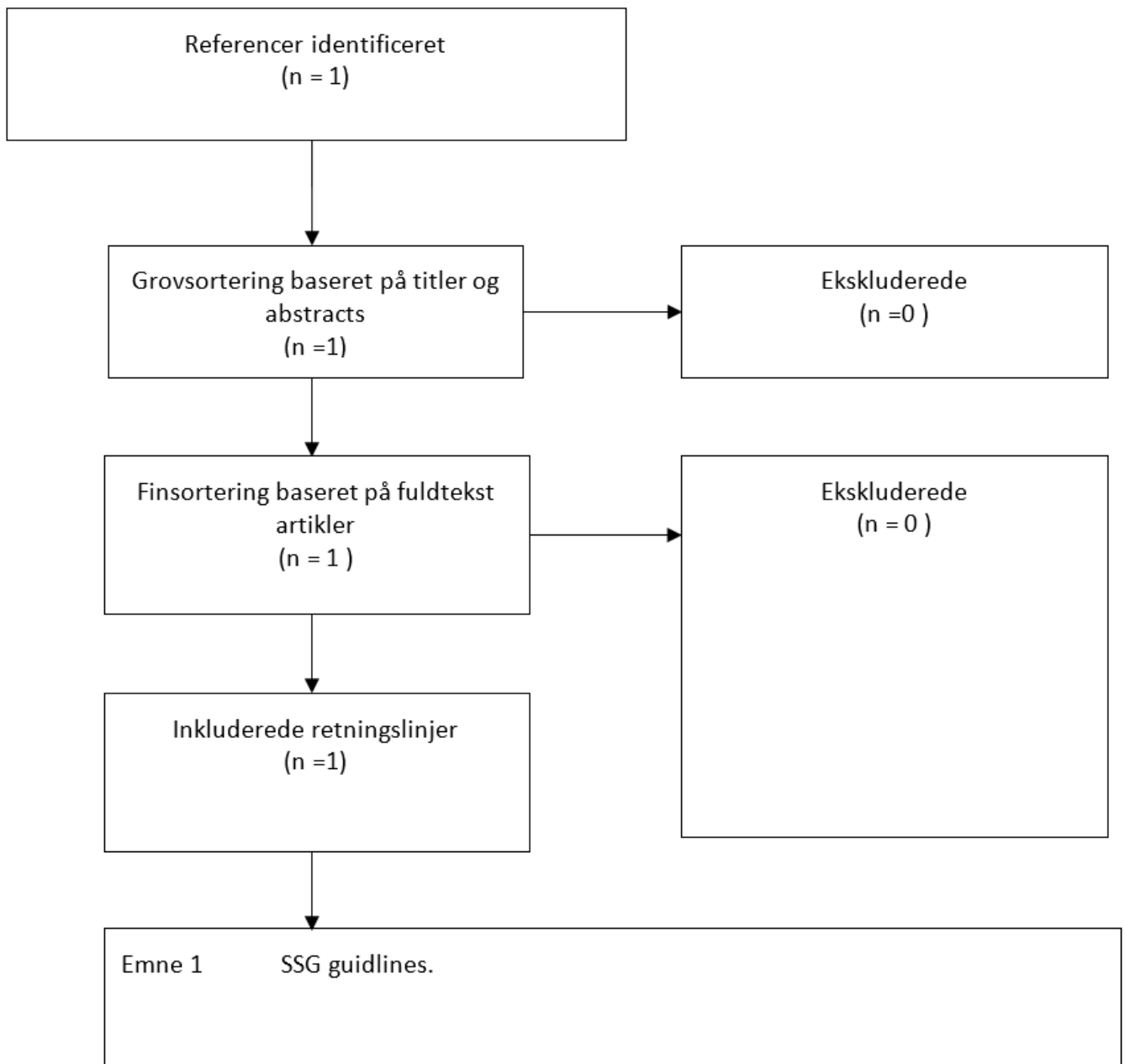
Flowchart – Primære studier

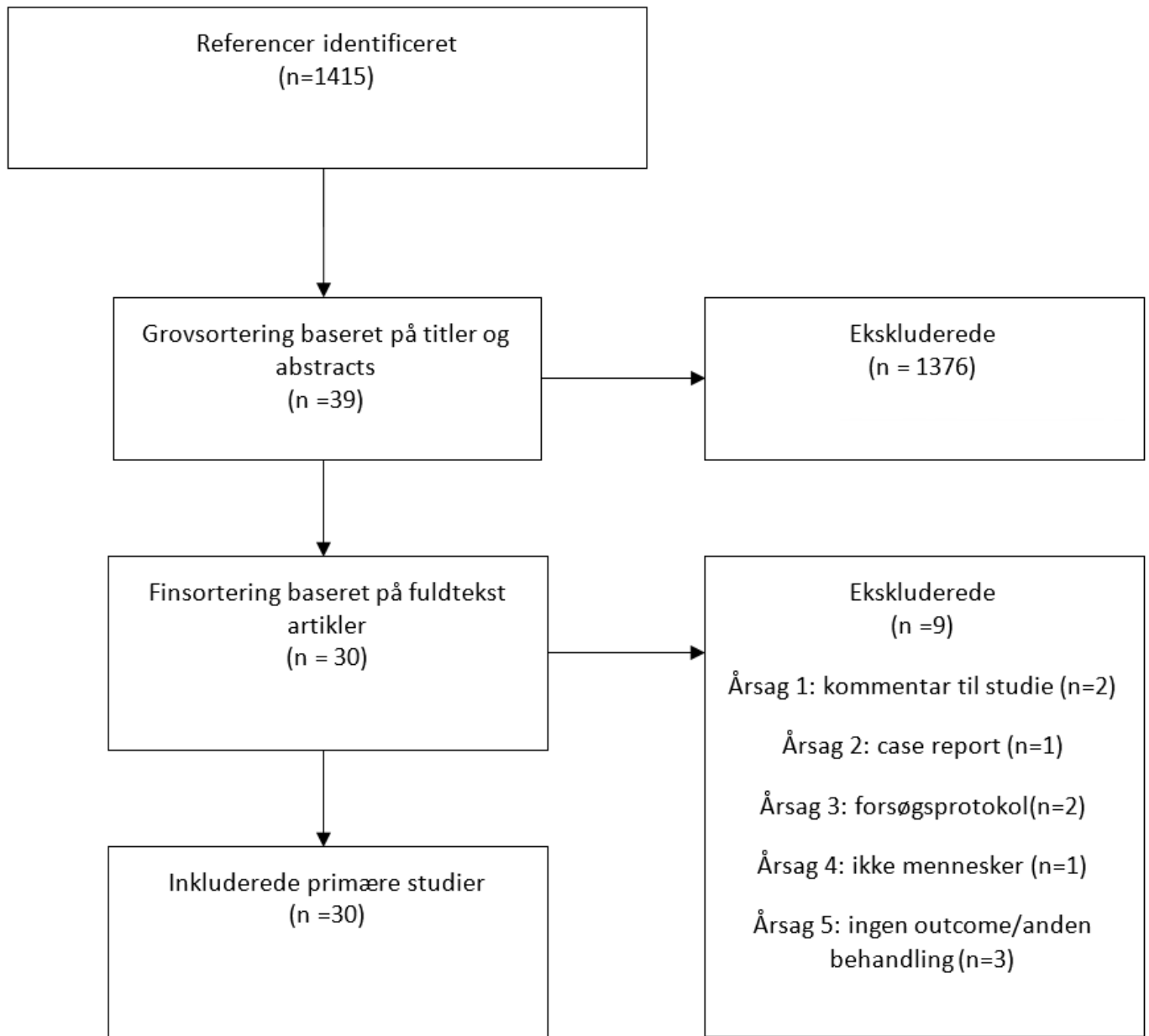


Flowchart – Primære studier fra 2018 (version 2)

Bilag 2b – Flowcharts immunterapi

Guidelines immunterapi



Flowchart – Primære studier immunterapi

Bilag 3 – Evidenstabel (Doxorubicin)

DMCG: DSG	Retningslinjens emne/titel: <i>Pallierende kemoterapi og targeteret behandling til patienter med bløddelssarkom - doxorubicin</i>							
Forfatter/ kilde	År	Undersøgelses- type/design	Under- søgel- sens kvalitet jf. Oxford	Intervention	Sammenlignings intervention	Patient- population	Resultater (outcome)	Kommentarer
<i>Steward WP et al.(1)</i>	1991	<i>Single-arm, fase 2</i>	2B	<i>Doxorubicin + ifosfamid</i>		STS (52)	ORR 43%	
<i>Wiklund TA et al.(2)</i>	1992	<i>Single-arm, fase 2</i>	2B	<i>Doxorubicin + ifosfamid, + vincristin + dacarbazine</i>		STS (37)	ORR 46% PFS 5 m OS 9.6 m	
<i>Edmonson JH et al.(3)</i>	1993	<i>Randomiseret, fase 3</i>	1B	<i>Doxorubicin</i>	<i>Doxorubicin+ ifosfamid eller doxorubicin + cispaltin mitocycin</i>	STS (279)	ORR dox 20%, ORR ifos+dox 34%	<i>Ingen overlevelses gevinst, men mere myelosuppression ved kombinationsbehandling er</i>
<i>Antman K et al(4)</i>	1993	<i>Randomiseret, fase 3</i>	1B	<i>Doxorubicin + dacarbazine (ad)</i>	<i>Doxorubicin + ifosfamid + dacarbazine (adi)</i>	STS (340)	ORRad 17% ORRadi 32% PFSad 4 m PFSadi 6 m OSad 13 m OSadi 12 m	
<i>Schütte J et al.(5)</i>	1993	<i>Single-arm, fase 2</i>	2B	<i>Doxorubicin + ifosfamid</i>		STS (203)	ORR 35% PFS 6.7 m OS 13.5 m	
<i>Santoro A et al.(6)</i>	1995	<i>Randomiseret, fase 3</i>	1B	<i>Doxorubicin (a)</i>	<i>CYADIC (cy) eller doxorubicin + ifosfamid (ai)</i>	STS (663)	ORR 24% ORRa 21.3 ORRcy 26.8% ORRai 25.2%	<i>Ingen forskel i OS mellem behandlinger OSa 52 uger OScy 51 uger OSai 55 uger</i>

<i>Sutton G et al.(7)</i>	1996	Single-arm, fase 2	2B	Doxorubicin + ifosfamid		Uterint leiomyosarkom (25)	ORR 30.3% OS 9.6 m	
<i>Jäger E et al.(8)</i>	1996	Single-arm, fase 2	2B	Doxorubicin + ifosfamid + Cisplatin + 5FU		STS (56)	ORR 30.3% PFS 4.5 m OS 11.8 m	
<i>Antman K et al.(9)</i>	1998	Single-arm, fase 2	2B	Doxorubicin + ifosfamid + dacarbazine mesna(MAID)		Rhabdomyosarkom (25)	ORR 62% PFS 10 m OS 15 m	
<i>Sandler A et al.(10)</i>	1998	Single-arm, fase 2		Doxorubicin + paclitaxel		STS (29)	ORR 22.2% PFS 4.5 m OS 10.2 m	Konklusionen som doxorubicin enkeltstof
<i>De Pas T et al.(11)</i>	1998	Single-arm, fase 2	3	Doxorubicin + ifosfamid		STS (23)	ORR 50% PFS 9 m	Meget toksisk
<i>Buesa JM et al.(12)</i>	1998	Single-arm, fase 2		Ifosfamide efterfulgt af doxorubicin		STS (27)	ORR 31% PFS 4.9 m OS14.7 m	2 linjebehandling
<i>Palumbo R et al.(13)</i>	1998	Single-arm, fase 2		Vincristine + doxorubicin + cyclophosphamide alternerende med ifosfamid + etoposid		STS (20)	ORR 45% OS10 m	2 CR, 7 PR
<i>Nielsen OS et al.(14)</i>	1999	Randomiseret, fase 3	1B	Doxorubicin	Epirubicin	STS (334)	PFSdox 3.7 m PFSEpi 3.3 m OSdox 10.5 m OSEpi 10.9 m	1. linjebehandling 2 dødsfald i epi gruppen (cardiotox) Ingen forskel i PFS og OS

Le Cesne A et al.(15)	2000	Randomiseret, fase 3	1B	Doxorubicin + ifosfamid	Doxorubicin (højdosis) + ifosfamid	STS (314)	PFSlav 4.7 m PFSHøj 7.2 m OSlav 13.1 m OSHøj 12.8 m	Ingen forskel i OS Mere toksisk ved højdosis dox
Verweij J et al.(16)	2000	Randomiseret, fase 2	2B	Doxorubicin	Docetaxel	STS (86)	ORR dox 30% ORR docetaxel 0%	Lukket før tid pga. ingen respondere til docetaxel – 1. linjebehandling
Comandone A et al.(17)	2000	Single-arm, fase 2	2B	Doxorubicin + ifosfamid		STS (42)	ORR 28% OS 7.6 m	
Edmonson JH et al.(18)	2002	Single-arm, fase 2	2B	Doxorubicin + mitocycin + cisplatin		Uterint leiomyosarkom (41)	ORR 23 % OS 6.3 m	
van Rijswijk RE et al.(19)	2003	Single-arm, fase 2	2B	Doxorubicin + ifosfamid + cisplatin		Uterint carcinosarkom (48)	ORR 56% OS 26 m	Meget toksisk
Kalofonos HP et al.(20)	2004	Single-arm, fase 2	3	Doxorubicin + cisplatin		STS (30)	ORR 16.7 % PFS 6 m OS 11.5 m	
Maurel J et al.(21)	2004	Single-arm, fase 2	2B	Sekventiel ifosfamid efterfulgt af doxorubicin		STS (60)	ORR 38% PFS 6 m	
Kawai A et al.(22)	2005	Single-arm, fase 2	2B	Alternerende ifosfamide og doxorubicin eller cyclofosfamid		Non-small round cell STS (42)	ORR 47.2%	Ingen PFS eller OS data
Leyvraz S et al.(23)	2006	Single-arm, fase 2	2B	Doxorubicin + ifosfamid (højdosis)		Uterint sarkom (37)	ORR 49% PFS 27.7 m OS 30.5 m	
Leyvraz S et al.(24)	2006	Single-arm, fase 2	2B	Doxorubicin (højdosis) + ifosfamid(højdos is)		STS (46)	ORR 48% PFS 16.2 m OS 19 m	Mange bivirkninger

Lorigan P et al.(25)	2007	Randomiseret, fase 3	1B	Doxorubicin	Ifosfamid	STS (326)	ORRdox 11.8% ORRifos 8.4%	Lukket præmaturt. Ingen gevinst af ifosfamid i forhold til doxorubicin ifosfamid mere toksisk
Fayette J et al.(26)	2009	Randomiseret, fase 3	2B	MAID	MAID højdosis	STS (162)	ORRmaid 35% ORRmaidhøj 38%	
Maurel J et al.(27)	2009	Randomiseret, fase 2	2B	Doxorubicin	Sekventiel doxorubicin + ifosfamid	STS (132)		Lukket præmaturt. Ingen forskel
De Pas T et al.(28)	2011	Single-arm, fase 2	2B	Doxorubicin + ifosfamid (kontinuert)		STS (34)	PFS 7.1	Meget toksisk
Italiano A et al.(29)	2012	Randomiseret, fase 2	2B	Doxorubicin	Paclitaxel (ugentlig)	Angiosarkom (117)	ORRdox 29% ORRpac 53% PFSdox 3 m PFSpac 5.8 m OSdox 5.5 m OSpac 10.3	
Demetri GD et al.(30)	2012	Randomiseret, fase 1 og 2	2B	Doxorubicin	Doxorubicin + conatumumab	STS (128)	PFSdox 6.4m PFStest 5.6 m	Ingen forskel
Gelderblom H et al.(31)	2013	Randomiseret, fase 2	2B	Doxorubicin	Brostallicin	STS(118)	PFSdox 6.1 m PFSbro 1.6 OSdox 13.2 m OSbro12.7 m	1. linjebehandling, ingen forskel i OS
Judson I et al.(32)	2014	Randomiseret, fase 3	1B	Doxorubicin	Doxorubicin + ifosfamid	STS (555)	PFSdox 4.6 m PFStest 7.4 m OSdos 12.8 m OSTest 14.3	Ingen signifikant forskel i OS. Kombinationsbehandling en gav mere toksicitet
Chawla SP et al.(33)	2015	Randomiseret, fase 2	2B	Doxorubicin	Aldoxorubicin	STS (126)	DCRdos 68% DCRaldox 77% PFSdox 2.7m PFSaldox 5.6m OSdox 14.3 m	ORRdox 5%, ORRaldox 26%

							OSaldox 15.8 m	
<i>Tap WD et al.(34)</i>	2016	Randomiseret, fase 2	2B	Doxorubicin	Doxorubicin + olaratumab	STS (133)	PFSdox 4.1 m PFSstest 6.6 m OSdox 14.7 m OSstest 26.5 m	ORRdox 11.9%, ORRtest 18.2%
<i>Seddon B et al.(35)</i>	2017	Randomiseret, fase 3	1B	Doxorubicin	Gemcitabin + docetaxcel	STS (257)	ORRdox 20% ORRgem 20% PFSdox 5.4 m PFSgem 5.5 m OSdox 17.8 m OSgem 15.7m	1.linjebehandling
<i>Tap WD et al.(36)</i>	2018	Randomiseret, fase 3	1B	Doxorubicin	Doxorubicin + evofosfamid	STS (640)	OSdox 19 m OSdoxevo 18.4 m	Ingen effekt
Grunwald V et al. (37)	2020	Randomiseret, fase 2	1B	Doxorubicin	Pazopanib	STS > 60 år ikke tidligere behandlet Dox (n=39) pazopanib (n=81)	ORRdox 15.4% ORRpazo 12.3% Ingen forskel i PFS eller OS.	Flere med neutopen feber ved dox behandlingen.
Tap W et al.(38)	2020	Randomiseret, fase 3	1B	Doxorubicin	Doxorubicin + olaratumab	STS 509	ORRdox 18.3% ORRdoxol 14% PFSdox 5.4 m PFSdoxol 6.8 m OSdox 19.7 m OSdosol 20.4m	
<i>D'Ambrosio et al.(39)</i>	2020	Retrospektiv kohorte studie	2B	Doxorubidin (dox) (n=115)	Doxorubicin + Ifosfamid (doxi) (n=71)	Leiomyos arkom. (303)	ORRdox 25.6% ORRdoxi 19.5% ORRdoxd 30.9% PFSdox 4.8 m PFSdoxi 8.2 m	Første linje behandling

					Doxorubicin + dacarbazine(doxd) (n=117)		PFSdoxd 9.2 m OSdox 30.3 m OSdoxi 21.9 m OSdoxd 36.8 m	
Toma S et al.(40)	2000	Single-arm, fase 2	2B	Caelyx		STS (25)	ORR 12% DCR 88%	2. linjebehandling
Judson I et al.(41)	2001	Randomiseret, fase 2	2B	Doxorubicin	Caelyx	STS (94)	ORRdox 9% ORRcalyx 10% PFSdox 2.73 m PFSscal 2.16 m OSdox 8.2 m OScal 10.6	Mindre toksisk behandling med caelyx.
Bafaloukos D et al.(42)	2004	Single-arm, fase 2	2B	Caelyx + paclitaxel		STS (42)	ORR 16% PFS 5.7 OS 13.2 m	
Sutton G et al.(43)	2005	Single-arm, fase 2	2B	Liposomalt doxorubicin		Uterint leiomyosar kom (35)	ORR 16.1%	Ingen PFS eller OS data

PR: Partiel respons som svare til en reduktion i tumor volumen på 30% eller derover.

DCR: Disease control rate som er patienter med partiel respons og stabil sygdom.

UPS: udifferentieret pleomorft sarkom

LMS: leiomyosarkom

DDLPS: dedifferentieret liposarkom

ASPA: alveolær soft part sarkom

CR: komplet respons

SD: stabil sygdom

PFR: progressions fri rate.

Pt: patienter

ORR: objektiv response rate (PR + CR)

ORRxxx: xxx er den behandling som outcome data relaterer til.

M: måneder

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Bilag 4 – Evidenstabel (Ifosfamid)

DMCG: DSG		Retningslinjens emne/titel: Pallierende kemoterapi og targeteret behandling til patienter med bløddelssarkom - ifosfamid						
Forfatter/ kilde	År	Undersøgelses-type/design	Under-søgel-sens kvalitet jf. Oxford	Intervention	Sammenlignin gs intervention	Patient-population	Resultater (outcome)	Kommentarer
Blackledge G et al.(1)	1992	Review		Ifosfamid		STS		Artiklen kunne ikke findes
Bramwell VH et al.(2)	1993	Randomiseret, fase 2	1B	Ifosfamid	Cyclophosp hamid	STS (171)	ORRcy 7.5% ORRifos 18%	1. linjebehandling
Frustaci S et al.(3)	1993	Single-arm, fase 2	2B	Ifosfamid + epirubicin		STS (64)	ORR 28% OS 13 m	Bedre i non-viscerale sarkomer
Chevallier B et al.(4)	1993	Single-arm, fase 2	2C	Ifosfamid + epirubicin		STS (30)	ORR 48% PFS 6.3 m OS 9.3 m	1. linjebehandling
Sutton GP et al.(5)	1994	Single-arm, fase 2	2C	Ifosfamid + mesna		Mixed mesodermale ovarie tumorer (31)	ORR 17.9%	2. linjebehandling
Le Cesne A et al.(6)	1995	Single-arm, fase 2	2C	Ifosfamid (høj dosis) +		STS (40)	ORR 22% PFS 8 m OS 12 m	2. linjebehandling, Leiomyosarkom virker resistent.

				tidligere behandlet med ifosfamid (lavdosis)				
Tursz T et al.(7)	1996	Single-arm, fase 2	2C	Ifosfamid (høj dosis)		STS (36)	ORR 33%	2. linjebehandling. Ingen leiomyosarkomer havde respons
Saeter G et al.(8)	1997	Single-arm, fase 2	2B	Ifosfamid + epirubicin		STS (92)	ORR 42%	
Palumbo R et al.(9)	1997	Single-arm, fase 2	2C	Ifosfamid (høj dosis)		STS (38)	ORR 39% OS 19 m	2. linjebehandling. Ingen leiomyosarkomer responderede (4 patienter med SD)
Reichardt P et al.(10)	1998	Single-arm fase 2	2B	Ifosfamid + epirubicin + filgrastim		STS (46)	ORR 52% OS 24 m	1. linjebehandling, toksicitet relativ høj
Yalçın S et al.(11)	1998	Single-arm, fase 2	2C	Ifosfamid + etoposide+ mesna		STS (26)	ORR 41.6% PFS 13.3 m	2. linjebehandling
Buesa JM et al.(12)	1998	Single-arm, fase 2	2B	Ifosfamid		STS (48)	ORR 37.7%	1. linjebehandling, høj toksicitet
Palumbo R et al.(13)	1999	Single-arm, fase 2	2B	Ifosfamid + epirubicin		STS (39)	ORR 59%	1. linjebehandling
Papai Z et al.(14)	2000	Single-arm, fase 2	2B	Etoposid+ ifosfamid+ cisplatin	Ingen	STS (104)	ORR 46% DCR 87%	
Nielsen OS et al.(15)	2000	Single-arm, fase 2	2B	Ifosfamid (høj dosis)		STS (124)	ORR 16% DCR 48% PFS 3.5 m OS 12.8 m	Leiomyosarkomer responderede ikke. 2. linjebehandling ORR 16% DCR 37% Meget toksicitet
Sutton G et al.(16)	2000	Randomiseret, fase 3	1B	Ifosfamid	Ifosfamid + cisplatin	Uterint carcinosarkom (224)	ORRifos 47% ORRifoscis 61% PFSifos 4 m	Høj toksicitet, lille gevinst på PFS, men ingen på OS

							PFSifoscis 5 m OSifos 7.6 m OSifoscis 9.4 m	
Serrone L et al.(17)	2001	Single-arm, fase 2	2C	Ifosamid + epirubicin		STS (22)	ORR 37% OS 15 m	
Serrone L et al.(18)	2001	Single-arm, fase 2	2B	Ifosamid + epirubicin		STS (44)	ORR 35% PFS 8.5 m OS 13.5 m	1. linjebehandling
van Oosterom AT et al.(19)	2002	Randomiseret, fase 2	1A	Ifosamid 1. linjebehandling	Ifosamid 2. linjebehandl ing	STS (182)	ORR1day 10 % ORR1L3day 24% ORR2I1day 6% ORR2I3day 8%	1. linjebehandling DCR1day 45%, DCR3day 53% 2. linjebehandling DCR1day 34% DCR3day 58%
Yalcin B et al.(20)	2004	Single-arm, fase 2	2B	Ifosamid (højdosis) + GM- CSF		STS (39)	PFS 7 m OS 10 m	
Siehl JM et al.(21)	2005	Single-arm, fase 2	2B	Ifosamid + liposomal daunorubicin		STS (40)	PFS 6 m OS 14 m	
Homesley HD et al.(22)	2007	Randomiseret, fase 2	1A	fosamid	Ifosamid + paclitaxel	Uterintcarinosarko m (214)	PFSifos 3.6 m PFSkomb 5.8 m OSfos 8.4 m OSkombi 14.5 m	
Lee SH et al. (23)	2011	Single-arm, fase 2	2C	Ifosamid (højdos)		STS (30)	ORR26% PFS 2.9 m OS 8.7 m	2. og 3. linjebehandling
Martin-Liberal J et al.(24)	2013	Retrospektivt studie	2C	Ifosamid		STS (34)	ORR 20 % DCR 48% PFS 4.2 OS 11.2	

PR: Partiel respons som svare til en reduktion i tumor volumen på 30% eller derover.

DCR: Disease control rate som er patienter med partiel respons og stabil sygdom.

UPS: udifferentieret pleomorft sarkom

LMS: leiomyosarkom

DDLPS: dedifferentieret liposarkom

ASPA: alveolær soft part sarkom

CR: komplet respons

SD: stabil sygdom

PFR: progressions fri rate.

Pt: patienter

ORR: objektiv response rate (PR + CR)

ORRxxx: xxx er den behandling som outcome data relaterer til.

M: måneder

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Bilag 5 – Evidenstabel (Trabectedin)

DMCG: DSG	Retningslinjens emne/titel: Pallierende kemoterapi og targeteret behandling til patienter med bløddelssarkom - trabectedin							
Forfatter/ kilde	År	Undersøgelses- type/design	Under- søgel-sens kvalitet jf. Oxford	Intervention	Sammenlignings intervention	Patient-population	Resultater (outcome)	Kommentarer
Le Cesne A et al.(1)	2004	Single-arm, fase 2	2B	ET-743	Ingen	STS (104)	ORR 8% PFS 3.5 m OS 9.2 m	
Yovine A et al.(2)	2004	Single-arm, fase 2	2B	Ecteinascidin-743	Ingen	ST (54)	ORR 4% PFS 1.9 m OS 12.8 m	
Garcia-Carbonero et al.(3)	2005	Single-arm, fase 2	2B måske C	Ecteinascidin-743	Ingen	STS (36)	ORR 17% PFS 1.6 m OS 15.8 m	
Roylance R et al.(4)	2007	Singelarm, fase 2	2B måske C	Trabectedin	Ingen	STS (21)	ORR 14% PFS 3.9 m OS 9.9 m	
Demetri GC et al.(5)	2009	Randomiseret, fase 2	A	Trabectedin	Ingen	Liposarkom og leiomyosarkom (270)	ORR 5.6% PFS 3.3 m OS 13.9 m	Randomisering ved infusion 24 h vs 3 h. 24 h er bedst
Monk BJ et al.(6)	2011	Single-arm, fase 2	2B	Trabectedin	Ingen	Uterint leiomyosarkom (20)	ORR 10% PFS 5.8 m OS 26.1 m	
Paz-Ares L et al.(7)	2012	Randomiseret, fase 2	2B	Trabectedin	Trabectedin + dexametason	STS (40)	ORR 3% PFS 2.1 OS 10.2 m	Samme overlevelse og PFS
Samuels BL et al.(8)	2013	Single-arm, fase 2	2B	Trabectedin	Ingen	STS (807)	ORR 5.9% OS 11.9 m	
Blay JY et al.(9)	2013	Single-arm, fase 2	2B	Trabectedin	Ingen	Liposarkom/leiomyosarkom (129)	ORR 6.4% PFS 4.4 m OS 17.4 m	Som 2. linje eller efterfølgende linjer. Bedst når givet som 2 linje.

<i>Blay JY et al.(10)</i>	2014	Randomiseret, fase 3	A	Trabectedin	Doxorubicin	Translokeret sarkom (121)	ORR 27% dox ORR 5,9% TRA	Som 1. linjebehandling. Doxorubicin bedst respons
<i>Pautier P et a.(11)</i>	2015	Single-arm, fase 2	2B	Trabectedin + doxorubicin	Ingen	Leiomyosarkom (109)	ORR 59.6% PFS 8.2 m OS 20.2 m	Som 1. linjebehandling
<i>Kawai A et al.(12)</i>	2015	Randomiseret, fase 2	2B	Trabectedin	Best supportive care	Translokeret sarkom (76)	PFS 5.6 m	2. linjebehandling
<i>Bui-Nguyen B et al.(13)</i>	2015	Randomiseret, fase 2	2B	Trabectedin	Doxorubicin	STS (133)	PFSdox 3.1 m PFStra 5.5 m	1. linjebehandling Lukket pga manglende superioreffekt af trabectedin
<i>Demetri GD et al.(14)</i>	2015	Randomiseret, fase 3	A	Trabectedin	Dacarbazin	Liposarkom/leiomyosarkom (518)	PFS 4.2 m OS 12.4 m	
<i>Martin-Broto J et al.(15)</i>	2016	Randomiseret, fase 2	2B	Doxorubicin	Doxorubicin + trabectedin	STS (115)	PFSdox 5.5 m PFStest 5.7 m	
<i>Hensley ML et al.(16)</i>	2017	Randomiseret fase 3	2A	Trabectedin	Dacarbazin	Leiomyosarkom uterint (232)	PFSdac 1.5 m PFStra 4 m OSdac 12.9 m OStra 13.4 m	Subgruppe analyse. 2. linjebehandling
<i>Buonadonna A et al.(17)</i>	2017	Single-arm, fase 4	2B	Trabectedin	Ingen	STS (219)	ORR 26.6% PFS 5.9 m	
<i>Takahashi M et al.(18)</i>	2017	Single-arm, fase 2	2B	Trabectedin	Ingen	Translokeret sarkom (66)	PFS 5.9 m OS 17.5 m	Specielt effektiv i myxoid/roundcell liposarkomer PFS 7.4
Gadducci A et al.(19)	2018	Single arm/randomiseret, fase 2	1B	Trabectedin	Ingen eller randomisering mod	Relaps af uterin leiomyosarkom Total 168	PFStra 4.1 m PFSg/d 6.9 m	

					<i>gemcitabien/doc etaxel hvis de ikke havde fået denne behandling før.</i>	<i>126 (45 pt randomiseret og 81 havde tidligere fået gem/doc) 42 pt til gem/doc</i>	<i>Ostra 20.6 m OSg/d 36.7 m</i>	
Jones R et al. (20)	2018	<i>Randomiseret, fase 3 Subgruppe analyse</i>	1B	<i>Trabectedin</i>	<i>Dacarbazine</i>	<i>577 patienter 131 over 65 år</i>	<i>ORRtra 9% PFStra 4.9 m Ostra 15 m ORRdec 3% PFSdec 2.5 m OSdec 8 m</i>	
Grignani E et al.(21)	2018	<i>Single arm, fase (1/2 studie</i>	2B	<i>Trabectedin + olaparib</i>		<i>50 STS</i>	<i>7/50 PR</i>	<i>Fase 2 er i gang.</i>
Patel S et al. (22)	2019	<i>Randomiseret, fase 3</i>	1B	<i>Trabectedin</i>	<i>Dacarbazine</i>	<i>Liposarkom eller leiomyosarkom patienter 577 Alle patienterne havde modtaget behandling før</i>	<i>Ostra 13.7 m OSdac 13.1 m</i>	
Grosso F et al. (23)	2020	<i>Single arm, fase 2</i>	2B	<i>Trabectedin som førstelinje</i>		<i>24 patienter, > 70 år</i>	<i>PFS 4 m OS 12 m</i>	
Hentschel L et al.(24)	2020	<i>Randomiseret</i>	1B	<i>Trabectedin</i>	<i>Trabectedin + intervention på Patient reported outcome.</i>		<i>OScontrol 389 dage OSinterven 648 dage</i>	
Le Cesne et al.(25)	2021	<i>Randomiseret, fase III</i>	1B	<i>Trabectedin Efter 1-3 tidligere behandlinger</i>	<i>Best supportive care</i>	<i>103 patienter</i>	<i>PFStra 3.1 m PFSbes 1.5 m</i>	<i>Livskvaliteten blev ikke forringet under behandlingen.</i>

PR: Partiel respons som svare til en reduktion i tumor volumen på 30% eller derover.

DCR: Disease control rate som er patienter med partiel respons og stabil sygdom.

UPS: udifferentieret pleomorft sarkom

LMS: leiomyosarkom

DDLPS: dedifferentieret liposarkom

ASPA: alveolær soft part sarkom

CR: komplet respons

SD: stabil sygdom

PFR: progressions fri rate.

Pt: patienter

ORR: objektiv response rate (PR + CR)

ORR_{xxx}: xxx er den behandling som outcome data relaterer til.

M: måneder

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Bilag 6 – Evidenstabel (Gemcitabin)

DMCG: DSG		Retningslinjens emne/titel: <i>Pallierende kemoterapi og targeteret behandling til patienter med bløddelssarkom - gemcitabin</i>						
<i>Forfatter/ kilde</i>	<i>År</i>	<i>Undersøgelses-type/design</i>	<i>Under-søgel-sens kvalitet jf. Oxford</i>	<i>Intervention</i>	<i>Sammenlignings intervention</i>	<i>Patient-population</i>	<i>Resultater (outcome)</i>	<i>Kommentarer</i>
<i>Patel SR et al.(1)</i>	2001	<i>Single-arm, fase 2</i>	2B	<i>Gemcitabin</i>		<i>STS (56)</i>	<i>ORR 18% PFS 3 m OS 13.9 m</i>	
<i>Hensley ML et al.(2)</i>	2002	<i>Single-arm, fase 2</i>	2B	<i>Gemcitabin + docetaxel</i>		<i>Leiomyosarkom (44)</i>	<i>ORR 53% PFS 5.6 m</i>	
<i>Okuno S et al. (3)</i>	2002	<i>Single-arm, fase 2</i>	2B	<i>Gemcitabin</i>		<i>STS (30)</i>	<i>ORR 3% PFS 2.1 m</i>	
<i>Svancarova L et al.(4)</i>	2002	<i>Single-arm, fase 2</i>	2B	<i>Gemcitabin</i>		<i>STS (32)</i>	<i>ORR 3.23% PFS 1.5 OS 8.9 m</i>	
<i>Okuno S et al. (5)</i>	2003	<i>Single-arm, fase 2</i>	2B	<i>Gemcitabin</i>		<i>STS (25)</i>	<i>PFS 13 m OS 15 m</i>	
<i>Von Buton G et al. (6)</i>	2006	<i>Single-arm, fase 2</i>	2B	<i>Gemcitabin</i>		<i>STS (48)</i>	<i>ORR 7% OS 6 m</i>	
<i>Maki RG et al. (7)</i>	2007	<i>Randomiseret, fase 2</i>	1B	<i>Gemcitabin</i>	<i>Gemcitabin + docetaxel</i>	<i>STS (122)</i>	<i>ORRgem 8% ORRkombi 16% PFSgem3 m PFSkombi 6.2 m</i>	<i>Mere toksicitet i kombinationsbehandlingen</i>

							OSgem11.5 m OSkombi17.9 m	
Losa R et al. (8)	2007	Single-arm, fase 2	2B	Gemcitabin + dacarbazine		STS (26)	PFS 9.25 m	
Bay JO et al. (9)	2007	Single-arm, fase 2	2B	Gemcitabin + docetaxel		STS (133)	OS 12.1 m	
Dileo P et al. (10)	2007	Single-arm, fase 2	2B	Gemcitabin + vinorelbin		STS (49)	PFS 3.4 m	
Hensley ML et al. (11)	2008	Single-arm, fase 2	2B	Gemcitabin + docetaxel		Uterin leiomyosarkom (42)	PFS 4.4 m OS 16 m	
Garcia-Del-Muro X et al. (12)	2011	Randomiseret, fase 2	1B	Dacarbazin	Gemcitabine + dacarbazine	STS (113)	PFS 2 dac PFS 4.2 kombi OS 8.2 dac PFS 16.8 kombi	
Lee EM et al. (13)	2011	Single-arm, fase 2	2B	Gemcitabin + docetaxel		STS (30)	PFS 2.5 m	
Stacchiotti et al. (14)	2012	retrospektivt		Gemcitabin +/- taxaner		Angiosarkom (25)	ORR 68% PFS 7 m OS 17 m	
Schmitt T et al. (15)	2013	Single-arm, fase 2	2B	Gemcitabin + docetaxel		STS (34)	PFS 8.6 m OS 22.4 m	
Luo Z et al. (16)	2015	Single-arm, fase 2	2B	Gemcitabin + vincristin + cisplatin.		STS (26)	ORR 23.1% PFS 4.8 m OS 15 m	
Martin-Liberal J et al. (17)	2018	Single-arm, fase 2	2B	Gemcitabine + sirolimus		STS (28)	ORR 0% PFS 1.85 m OS 9.2 m	Tidligere behandlet med dox
Pautier et al. (18)	2020	Single-arm, fase 2	2B	Gemcitabine + pazopanib		STS (106)	PFS 6.5 m OS 22.4 m	

PR: Partiel respons som svare til en reduktion i tumor volumen på 30% eller derover.

DCR: Disease control rate som er patienter med partiel respons og stabil sygdom.

UPS: udifferentieret pleomorft sarkom

LMS: leiomyosarkom

DDLPS: dedifferentieret liposarkom

ASPA: alveolær soft part sarkom

CR: komplet respons

SD: stabil sygdom

PFR: progressions fri rate.

Pt: patienter

ORR: objektiv response rate (PR + CR)

ORRxxx: xxx er den behandling som outcome data relaterer til.

M: måneder

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Bilag 7 – Evidenstabel (Kemoterapi andet)

DMCG: DSG		Retningslinjens emne/titel: <i>Pallierende kemoterapi og targeteret behandling til patienter med bløddelssarkom – kemoterapi andet</i>						
<i>Forfatter/ kilde</i>	<i>År</i>	<i>Undersøgelses-type/design</i>	<i>Under-søgel-sens kvalitet jf. Oxford</i>	<i>Intervention</i>	<i>Sammenlignings intervention</i>	<i>Patient-population</i>	<i>Resultater (outcome)</i>	<i>Kommentarer</i>
<i>Jelić S et al.(1)</i>	<i>1990</i>	<i>Single-arm</i>	<i>2C</i>	<i>Epirubicin + cisplatin</i>		<i>STS (35)</i>	<i>ORR 57.1% OS 4 m</i>	<i>1. linjebehandling</i>
<i>Lopez M et al.(2)</i>	<i>1991</i>	<i>Single-arm</i>	<i>2B</i>	<i>Epirubicin + dacarbazine</i>		<i>STS (56)</i>	<i>ORR 48% OS 14 m</i>	<i>Cardiotoksisk</i>

Jelić S et al.(3)	1997	Randomiseret	1B	Epirubicin (høj)	Epirubicin (høj) + cisplatin	STS (106)	ORRepi 29% ORRepicis 54%	Kombinationsbehandlingen mere toksisk
Jelić Set al.(4)	2000	Randomiseret	1A	Epirubicin (høj) + cisplatin	Epirubicin (lav) + cisplatin	STS (159)	ORRepihøj 53% ORRepilav 30% OShøj 14 m OSlav 11 m	Samme toksicitet
Van Hoesel OG et al. (5)	1994	Single-arm, fase 2	2C	Docetaxel	Ingen	STS (29)	ORR 17%	
Kostler WJ et al.(6)	2001	Single-arm, fase 2	2C	Docetaxel	Ingen	STS (27)	ORR 15% PFS 2.4 m OS 7.7	
Balcerzak SP et al.(7)	1995	Single-arm, fase 2	2B	Paclitaxel	Ingen	STS (48)	ORR 12.5%	
Casper ES et al.(8)	1998	Single-arm, fase 2	2C	Paclitaxel	Ingen	STS (28)	ORR 7% PFS 3.5 m	
Sutton G et al.(9)	1999	Single-arm, fase 2	3	Paclitaxel	Ingen	Uterint leiomyosarkom (24)	ORR 9.1 % DCR 33.1 %	
Curtin JP et al.(10)	2001	Single-arm, fase 2	2B	Paclitaxel	Ingen	Uterint carcinosarkom (53)	ORR 18.2%	
Gallup DG et al.(11)	2003	Single-arm, fase 2	2B	Paclitaxel	Ingen	Uterint leiomyosarkom (53)	ORR 8.4% DCR 31.3 % PFS 1.5 m OS 12.1 m	
Penel N et al.(12)	2008	Single-arm, fase 2	2C	Ugentlig paclitaxel	Ingen	Angiosarkom (30)	ORR 18% PFS 4 m OS 8 m	

Powell MA et al.(13)	2010	Single-arm, fase 2	2B	Paclitaxel + carboplatin	Ingen	Uterint carcinosarkom (45)	ORR 54% PFS 7.6 m OS 14.7 m	
Ray-Coquard IL et al.(14)	2015	Randomiseret, fase 2	2B	Paclitaxel	Paclitaxel + bevacizumab	Angiosarkom (52)	ORRpax 45.8% ORRpaxb 28% PFSpax 6.6 m PFSpaxb 6.6 m OSpax 19.5m OSpaxb 15.9 m	
Goldstein D et al.(15)	1990	Single-arm, fase 2	2B	Carboplatin	Ingen	STS (50)	ORR 16%	
Thigpen JT et al.(16)	1992	Single-arm, fase 2	2B	Cisplatin	Ingen	Uterint sarkom (96)	ORR 9% DCR 70% OS 7 m	
Keohan ML et al.(17)	1997	Single-arm, fase 2	3	Cisplatin + vinblastin	Ingen	STS (20)	ORR 0%	Ingen effekt
Blay JY et al.(18)	2015	Randomiseret, fase 3	1A	Cisplatin	Cisplatin + ombrabulin	STS (355)	ORRcis 1% ORRtest 4% PFScis 1.41 m PFStest 1.54 m OScis 9.33 m OStest 11.43 m	Ingen effekt
Buesa JM et al.(19)	1991	Single-arm, fase 2	2B	Dacarbazin	Ingen	STS (50)	ORR 18%	2. linjebehandling
Licht JD et al.(20)	1994	Single-arm, fase 2	3	Etoposid	Ingen	STS (25)	ORR 4%	
Currie JL et al.(21)	1996	Single-arm, fase 2	2C	Darcabazin + etoposide+ hydroxyurea	Ingen	Uterint sarkom (33)	DCR 15.7%	
Thigpen T et al.(22)	1996	Single-arm, fase 2	3	Etoposid	Ingen	Uterint leiomyosarkom (28)	PFS 2.1 m OS 9.2 m	

Rose PG et al.(23)	1998	Single-arm, fase 2	3	Etoposid	Ingen	Uterint leiomyosarkom (26)	ORR 6.8%	
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PR: Partiel respons som svare til en reduktion i tumor volumen på 30% eller derover.

DCR: Disease control rate som er patienter med partiel respons og stabil sygdom.

UPS: udifferentieret pleomorft sarkom

LMS: leiomyosarkom

DDLPS: dedifferentieret liposarkom

ASPA: alveolær soft part sarkom

CR: komplet respons

SD: stabil sygdom

PFR: progressions fri rate.

Pt: patienter

ORR: objektiv response rate (PR + CR)

ORRxxx: xxx er den behandling som outcome data relaterer til.

M: måneder

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Bilag 8 – Evidenstabel (Targeteret)

DMCG: DSG		Retningslinjens emne/titel: Pallierende kemoterapi og targeteret behandling til patienter med bløddelssarkom – targeteret behandling						
Forfatter/ kilde	År	Undersøgelses-type/design	Under-søgel-sens kvalitet jf. Oxford	Intervention	Sammenlignings intervention	Patient-population	Resultater (outcome)	Kommentarer
Sleijfer S et al.(1)	2009	Single-arm, fase 2	2B	Pazopanib	Ingen	STS (142)	ORRleio 44%, ORRsyn 49% ORRother 39%	Adipocystisk STS lukket. PFSleio 3.0 m, PFSsyn 5.4 m, PFSoth 3.0m, OSleio 11.8 m, OSSyn 10.3 m, OSoth 10 m
van der Graaf WT et al. (2)	2012	Randomiseret, fase 3	1B	Pazopanib	Placebo	STS (372)	ORRpazo 6% ORRpla 0% PFSpazo 4.6 m PFSpla 1.6 m OSpazo 12.5 m OSpla 10.7 m	DCRpazo 63% DCRpla 38%
Benson C et al. (3)	2016	Subgruppe analyse	2B	Pazopanib	Ingen	Uterint sarkom (44)	ORR 11.4% DCR 68.2% PFS 3 m OS 17.5 m	
Kollár A et al. (4)	2016	Retrospektivt	3	Pazopanib	Ingen	Vaskulært sarkom (angiosarkom, epitheloidt hemangioendoth	ORR 23.1 % DCR 54.3% PFS 3 m OS 9.9 m	

						<i>eliom og intimal sarkom) (52)</i>		
<i>Samuels BL et al. (5)</i>	2017	<i>Single-arm, fase 2</i>	2B	<i>Pazopanib</i>	<i>Ingen</i>	<i>Liposarkom (41)</i>	<i>ORR 2.4% DCR 44% PFS 4.4 m OS 12.6 m</i>	
<i>Subbiah V et al. (6)</i>	2018	<i>Single-arm, fase 2</i>	2C	<i>Pazopanib + trametinib (MEK hæmmer)</i>	<i>Ingen</i>	<i>STS (25)</i>	<i>ORR 8% PFS 2.3 m</i>	
Sharma A et al.(7)	2019	<i>Retrospektiv opgørelse</i>	4	<i>pazopanib</i>		<i>STS (33)</i>	<i>ORR 6% PFS: 5 m OS: 18 m</i>	
Mir O et al.(8)	2019	<i>Retrospektiv opgørelse</i>	4	<i>Pazopanib (pazo)</i>	<i>Pazopanib + syrepumpehæmmer (pazo+)</i>	<i>STS(333) 59 fik pazopanib og syrepumpehæmmer</i>	<i>PFSpazo 4.6 m PFSpazo+ 2.8 m OSpazo 12.6 m OSpazox 8 m</i>	
Vos M et al.(9)	2019	<i>Retrospektiv analyse</i>	2B	<i>pazopanib</i>		<i>STS (259)</i>	<i>Ingen association mellem bivirkninger og outcome.</i>	
Hirbe A C et al.(10)	2020	<i>Single-arm, fase 2</i>	2B	<i>Pazopanib Første linje behandling</i>		<i>STS patienter som ikke er kandidater til kemoterapi (56)</i>	<i>DCR: 39% PFS: 3.7 m OS 14.2 m</i>	
Nishida Y et al. (11)	2021	<i>Single-arm-fase 2</i>	2B	<i>Pazopanib</i>		<i>Malign perifer nerve skede tumor (MPNST) 12 patienter</i>	<i>PFS 5.4 m OS 10.6 m</i>	
<i>Schöffski P et al. (12)</i>	2011	<i>Single-arm, fase 2</i>	2B	<i>Eribulin</i>	<i>Ingen</i>	<i>STS (128)</i>	<i>ORRradi 6%, ORRleio 0%, ORRsyn 5% ORRother 4%</i>	<i>DCR dedifferentieret liposarkom 47.6 %, PFS adipocystisk 2.6 m PFS leiomyosarkom 2.9 m PFS synovial sarkom 2.6 m</i>

								<i>PFS andre 2.1 m</i>
<i>Schöffski P et al. (13)</i>	2016	<i>Randomiseret, fase 3</i>	1B	<i>Eribulin</i>	<i>Dacarbazin</i>	<i>Leiomyosarkom/ liposarkom (452)</i>	<i>ORReri 4% ORRdac 5% PFSeri 2.6 m PFSda 2.6 m OSeri 13.5 m OSeri 11.5 m</i>	<i>DCReri 56%, DCRdac 53% Effekt ved liposarkom, ved leiomyosarkom var dacarbazin lige så godt</i>
<i>Demetri GD et al. (14)</i>	2017	<i>Randomiseret, fase 3</i>	1B	<i>Eribulin</i>	<i>Dacarbazin</i>	<i>Liposarkom (143)</i>	<i>DCReri 64% DCRdac 44.4% PFSeri 2.9 m PFSdac 1.7 m OSeri 15.6 m OSdac 8.4 m</i>	
<i>Kawai A et al. (15)</i>	2017	<i>Single-arm, fase 2</i>	2B	<i>Eribulin</i>	<i>Ingen</i>	<i>STS (52)</i>	<i>PFSlipo/leio 5.5 m</i>	
Blay JY et al.(16)	2019	<i>Randomiseret, fase 3 Subgruppe analyse</i>	1B	<i>Eribulin</i>	<i>Dacarbazin</i>	<i>Leiomyosarkom 309 patienter 42% uterin leiomyosarkom</i>	<i>ORReri 5% ORRdac 7% PFSeri 2.2m PFSdac 2.6 m OSeri 12.7 m OSdac 13.0 m</i>	
<i>Bramwell VH et al. (17)</i>	1995	<i>Single-arm, fase 2</i>	2C	<i>Topotecan (topoisomerase I hæmmer)</i>	<i>Ingen</i>	<i>STS (22)</i>	<i>ORR 10.3%</i>	<i>Ingen effekt</i>
<i>Miller DS et al. (18)</i>	2000	<i>Single-arm, fase 2</i>	2B	<i>Topotecan</i>	<i>Ingen</i>	<i>Uterint leiomyosarkom (26)</i>	<i>ORR 11% DCR 19%</i>	<i>Ingen effekt</i>
<i>Budd GT et al. (19)</i>	2002	<i>Single-arm, fase 2</i>	3	<i>Topotecan</i>	<i>Ingen</i>	<i>STS (22)</i>	<i>ORR 0% OS 12 m</i>	
<i>Miller DS et al. (20)</i>	2005	<i>Single-arm, fase 2</i>	2B	<i>Topotecan</i>	<i>Ingen</i>	<i>Uterint sarkom carcinosarkoma (27)</i>		<i>Ingen effekt</i>

<i>Maki et al. (21)</i>	2009	Single-arm, fase 2	2B	Sorafenib	Ingen	STS (145)	ORR angio 14% PFS 3.2 m OS 14.3 m	Aktiv ved angiosarkom, men begrænset aktivitet ved andre. PFS angio 3.8 m OS, angio 14.9 m Måske lidt effekt i leiomyosarkom
<i>von Mehren M et al. (22)</i>	2011	Single-arm, fase 2	2B	Sorafenib	Ingen	Vaskulært sarkom, liposarkom, leiomyosarkom (51)		
<i>Ray-Coquard I et al. (23)</i>	2012	Single-arm, fase 2	2B	Sorafenib	Ingen	Angiosarkom (41)		
<i>Santoro A et al. (24)</i>	2013	Single-arm, fase 2	2B	Sorafenib	Ingen	STS (101)	ORR 14.5% DCR 47.4% PFS 4.2 m OS 11.9 m	Særlig effektiv ved leiomyosarkom
<i>D'adamo et al. (25)</i>	2018	Single-arm, fase 2	2B	Sorafenib + dacarbazine	Ingen	STS (37)	DCR 46% PFS 3.1 m OS 13.2 m	
Garcia Del Muro X et al.(26)	2018	Single-arm, fase 2	2B	Sorafenib + ifosfamide.		STS (34)	ORR: 17% DCR:49% PFS:4.8 m OS 16.2 m	
<i>Chawla SP et al. (27)</i>	2012	Single-arm, fase 2	2B	Ridaforolimus (mTOR inhibitor)	Ingen	STS (212)	DCR 28.8 % PFS 3.8 m OS 10 m	
<i>Demetri GD et al. (28)</i>	2013	Randomiseret, fase 3	1B	Placebo	Ridaforolimus (mTOR inhibitor)	STS (711)	DCRrida 40.6% DCRplac 28.6% PFSrida 4.13 m	Beskedent effekt med stort studie

							PFSplac 3.4 m	
<i>Mir O et al. (29) Regosarc</i>	2016	Randomiseret	1B	Placebo	Regorafenib	STS (182)	ORR 11% DCR 67% PFSrego 2.9 m PFSplac 1.0 m	Liposarkom DCR 45 % ORR 0% Liposarkom PFSrego 1.1 m Liposarkom PFSplac 1.7 m Leiomyosarkom DCR 86%, ORR 0% Leiomyosarkom PFSrego 3.7 m Leiomyosarkom PFSplac 1.8 m Synovial DCR 77%, ORR 8% Synovial PFSrego 5.6 m Synovial PFSplac 1.0 m
Brodowicz T et al.(30) Regosarc	2018	Randomiseret. Cross over	1B	placebo	ragorafenib	STS (139) Non-adipocytisk sarkomer	81% af patienterne crossed-over til ragorafenib. Ingen forskel i OS.	
Marrari A et al.(31)	2020	Single arm, fase 2	2B	ragorafenib		STS (21)	ORR: 4.7% DCR: 62% PFS 3.8 m OS 14.8 m	
Panel N et al.(32)	2020	Randomiseret, fase 2	1B	placebo	ragorafenib	STS pt som tidligere er blevet behandlet med kemoterapi og pazopanib (non adipocytisk STS) (37)	PFSplac 1.1 m PFSpazo 2.1 m OSplac 8.2 m OSpazo 17.8 m	

Riedel RF et al.(33)	2020	Randomiseret, fase 2	1B	placebo	ragorafenib	Liposarkom, vel differentieret var ekskluderet. (48)	PFSpla 2.07 m PFSrago 1.87 m OSpla 4.89 m OSrago 6.46 m	
Liao Z et al. (34)	2019	Single-arm, fase 2	2B	Apatinib (VEGFR2 hæmmer)		STS (59)	ORR 115% DCR 58% PFS 7.9 m OS 17 m	
Schoffski P et al.(35)	2018	Single arm, fase 2	2B	Crizotinib		Alveolar soft part sarkom ASPS (48) opdelt i to subkohorter afhængig af om det havde et TFE3 re-arrangement	+rearrangement (40 pt) ORR:2.5% DCR:90% PFS (1 år): 37.5% OS (1 år):97.4% -rearrangement (4 patienter) ORR: 25% DCR: 100% PFS (1 år): 50% OS(1 år): 75%	
Veitch Z et al.(36)	2019	Single arm, fase 2	2B	ENMD-2076 aurora A kinase hæmmer		STS (25)	ORR 9% PFS 2.5 m Os 14.1 m	
Gounder M et al.(37)	2020	Single-arm, fase 2	2B	Tazemetostat	ingen	Epithelioid sarkom (62)	ORR. 15% PFS5.5 m OS 19 m	

PR: Partiel respons som svare til en reduktion i tumor volumen på 30% eller derover.
DCR: Disease control rate som er patienter med partiel respons og stabil sygdom.

UPS: udifferentieret pleomorft sarkom

LMS: leiomyosarkom

DDLPS: dedifferentieret liposarkom

ASPA: alveolær soft part sarkom

CR: komplet respons

SD: stabil sygdom

PFR: progressions fri rate.

Pt: patienter

ORR: objektiv response rate (PR + CR)

ORR_{xxx}: xxx er den behandling som outcome data relaterer til.

M: måneder

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Bilag 9 – Evidenstabel (Check-point hæmmer)

DMCG: DSG		Retningslinjens emne/titel: Pallierende kemoterapi og targeteret behandling til patienter med bløddelssarkom – check point hæmmer						
Forfatter/ kilde	År	Undersøgelses-type/design	Under-søgel-sens kvalitet jf. Oxford	Intervention	Sammenlignin gs intervention	Patient-population	Resultater (outcome)	Kommentarer
Maki et al.(1)	2013	Single arm, fase 1	4	Ipilimumab (anti-CTLA4 hæmmer)	ingen	7 synovial sarkom patienter	Ingen effekt	
Merchant et al.(2)	2016	Single arm, fase 1	2b	ipilimumab	ingen	33 patienter, 17 havde sarkom	3 sarkom patienter havde stabilisering af sygdommen, 1 osteosarkom, en med clear celle sarkom og en med synovial sarkom	
Weiss G et al.(3)	2017	Single arm, fase 1b 6 behandlingsarme	4	Undersøge kombinationen af pembrolizumab og forskellige former for kemoterapi		Solide tumorer 49 patienter. 7 sarkom patienter med avanceret sygdom	Patienter som havde gavn 1 Liposarkom 1 Uterin leiomyosarkom Følgende havde ikke gavn 1 Clear celle sarkom 2 synovial sarkom 1 fibromyxoid sarkom 1 malign fibrøs histiocytom	Alle sarkom patienterne havde modtaget op mod 4 linjer kemoterapi forud for behandlingen.
Schur S et al.(4)	2017	Retrospektiv opgørelse		Pembrolizumab behandling		18 patienter	Outcome data forekommer ikke	
Tawbi HA et al.(5)	2017	Single arm, fase 2	1c	Effekten af pembrolizumab ved sarkom patienter		Metastatisk sarkom sygdom. 86 patienter og 80 kunne evalueres for respons 40 patienter med bløddelssarkom 40 patienter med knoglesarkom	Leiomyosarkom 6/10 pt havde SD: DCR=60% UPS 1/10 havde CR, 3/10 havde PR, 3/10 havde SD, DCR=70%. Ved 12 uger var PFR 70% Liposarkom 2/10 PR, 4/10 SD DCR=60%. ved 12 uger var PFR=60% Synovial sarkom 1/10 PR, 2/10 SD. DCR=30%	Der var ingen korrelation mellem PD-L1 udtrykket og respons Burgess, 2017.

Ben-Ami et al.(6)	2017	Single arm, fase 2	4	Checkpoint hæmmer (nivolumab) til leiomyosarkom		12 patienter med uterin leiomyosarkom	Ingen responderede på behandlingen.	
Toulmonde M et al.(7)	2018	Single arm, fase 2	1c	Effect af PD-1 hæmning sammen med lavdosis kemoterapi cyclophosphamide		57 sarkom patienter Leiomyosarkom (15 pt) UPS (16 pt) Andre (16 pt) GIST (10 pt)	Stabil sygdom for 3 leiomyosarkomer, 7 UPS, 8 indenfor gruppen andre og 3 gist.	
D-Angelo et al.(8)	2018	Single arm, fase 2	1c	Behandling med nivolumab (PD-1 hæmmer) og ipilimumab (CTLA-4 hæmmer)		85 patienter 76 patienter blev evalueret	Nivolumab: ORR 5% Nivolumab+ipilimumab: ORR 16%	Repondere var blandt UPS, mangiosarkom og myxofibrosarkom.
Wilky et al.(9)	2019	Single arm, fase 2	2b	Axitinib (VEGFR receptor tyrosin kinase hæmmer) sammen med pembrolizumab		33 sarkom patienter. 12 med alveolar soft-part sarkom. 2 pt ikke uterin leiomyosarkom 3 uterin leiomyosarkom 5 UPS 2 liposarkomer 3 kan ikke evalueres 6 andre	ASPS: DCR 73% Partiel repons: 1 pt med epitheloidt sarkom 1 pt med leiomyosarkom (ikke uterin) Stabil sygdom (mindre end 30% reduktion) 1 leiomyosarkom (ikke uterin) 3 UPS 1 synovial sarkom	Meget blandet gruppe af histologiske undertyper Total 2 leiomyosarkomer (ikke uterine),
Le Cesne et al.(10)	2019	Single arm, fase 2	2b	Pembrolizumab sammen med lavdosis kemoterapi cyclophosphamide		17 osteosarkom patienter 15 kunne evalueres	PR 1 patient. 6 måneders PFS =13.3% (1.7-40% 95% CI)	Begrænset aktivitet ved osteosarkom.
Florou et al.(11)	2019	Retrospektiv analyse	4	Pooled data fra 1 pembrolizumab + axitinib studiet (1 pt) 2 patienter behandlet med CTLA-4 hæmmer		7 patienter med spredt angiosarkom	PR: 71% CR 1/7 patienter.	

				4 patienter med pembrolizumab				
Kelly et al.(12)	2019	Single arm, fase 2	2b	Pembrolizumab sammen med epacadostat (IDO1 hæmmer)		29 patienter Leiomyosarkom (17%), UPS (17%) myxofibrosarkom (7%) liposarkom (11%), angiosarkom(3%)	PR: 1 leiomyosarkom patient SD: 13 patienter. Median PFS: 8 måneder (95%CI: 6.9-26.7)	
Tian et al.(13)	2020	Retrospektiv analyse	2c	Pembrolizumab sammen med kemoterapi (doxorubicin) i behandling af sarkomer		21 patienter med spredt bløddelssarkom	ORR: 47.6 % DCR: 71.4% Median PFS: 6 måneder (95% CI 2-8 måneder)	Ikke de store bivirkninger til behandlingen.
Quiroga et al.(14)	2020	Retrospektiv analyse	2c	Behandling med nivolumab eller pembrolizumab		56 patienter: Liposarkom 11 Leiomyosarkom 7 Synovial sarkom 4 Chordom 4 Tencelle sarkom 4 Osteosarkom 3 UPS 3 Andre 20	ORR: 11.5%	Kun 26 patienter kunne evalueres.
Pollack S et al.(15)	2020	Single arm, fase 1/2	1c	Behandling med doxorubicin i kombination med pembrolizumab		37 patienter	ORR:19% PFS median: 8.1 måneder (95% CI 7.6-10.8) 2/3 UPS og 2/4 dedifferentieret liposarkomer havde PR	Patienterne tålte behandlingen godt. Mange forskellige histologiske typer var inkluderet
Naing et al.(16)	2020	Single arm, fase 2	1c	Behandlingen med pembrolizumab		127 patienter Antallet af sarkom patienter kan ikke bestemmes ud fra artiklen.		
Monga V et al.(17)	2020	Retrospektiv	2c	Behandling med immunterapi		88 sarkom patienter med forskellige histologi Totale antal UPS=25 patienter	CR: 1 UPS patient PR: 20 patienter (7 UPS, 9 leiomyosarkomer, 1 ASPS, 3 andre) SD: 28 patienter	
Kelly CM et al.(18)	2020	Single arm, fase 2	2b	T-VEC (vaccine) i kombination		20 sarkom patienter med metastatiske sygdom	ORR: 30%. DCR:70%	Ingen alvorlig bivirkninger

				med pembrolizumab				Mange forskellige histologiske diagnoser
Italiano A et al. (19)	2020	Meta-analyse	2a	Fase II forsøg som har undersøgt effekten af PD1 eller PDL1 hæmmere i bløddelsarkomer		384 patienter med sarkom, 153 af disse blev kun behandlet med PD1 eller PDL1 hæmmere	ORR (monoterapi): 18,7% DCR (monoterapi): 63,6% UPS: ORR 15,7%, DCR: 50,5% LMS: ORR 6,9%, DCR: 54,1% DDLPS: ORR 7,3% DCR: 54,5% ASPS: ORR 48,8%, DCR: 80,5%	Indenfor de forskellige undertyper er der forskellige ORR og DCR
Callaghan CM et al. (20)	2020	Retrospektiv analyse	4	Undersøgelse af strålebehandling sammen med PD1 hæmmer		5 patienter 10 metastaser behandlet	50% metastaser med komplet respons 10% med PR 30% med SD	Ingen alvorlige bivirkninger
Martin-Broto et al. (21)	2020	Single arm, fase 1b/2	2b	Undersøgelse af checkpoint hæmmer med tyrosin kinase hæmmer sunitinib		68 patienter med bløddelsarkom	6 måneder PFS: 48% (95%CI 41-55%)	
Zhou et al. (22)	2020	Retrospektiv analyse	2c	Undersøgelse af checkpoint hæmmere nivolumab og ipilimumab i kombination.		38 patienter med bløddelssarkom. Leiomyosarkom 9 Liposarkom 6	ORR: 15% DCR: 34% PFS 2.7 måneder (95%CI:2.3-4.5) For patienter med CR og PR PFS: 23.4 måneder (95% CI: 7-?)	Behandlingen blev tålt god.
Geoerger et al. (23)	2020	Single arm, fase 1/2	1c	Undersøgelse af atezolizumab en PD-L1 hæmmer		87 patienter inkluderet(alle under 18 år). 42 patienter havde sarkom Primært Ewing sarkom (n=11), non-rhabdomyosarkom (n=9), osteosarkom (n=10), Rhabdomyosarkom (n=10)	2 Ewing sarkom patienter havde stabil sygdom og en malignt rhabdoid tumor havde komplet respons.	

						Malign rhabdoid tumour (n=3)		
Geoerger et al. (24)	2020	Single arm fase 1/2	1c	Pembrolizumab behandling til PD-L1 positive sarkomer + mange andre diagnoser		155 patienter inkluderet. Sarkomer udgjorde 21% (n=33).	PR: 2 sarkom patienter SD: 1 sarkom patienter.	
Scheinberg T et al.(25)	2021	Retrospektiv analyse	2c	Analys af PD-1 hæmmer ved unge og unge voksne med sarkom		18 patienter Antal patienter som kunne evalueres	CR: 7% PR: 7% SD: 7% DCR: 21%	
Livingston MB et al.(26)	2021	Single arm, fase 2	2b	Doxorubicin og pembrolizumab som kombinations behandling		30 patienter, bløddelssarkomer	ORR 36,7 % (95% CI 19-9-56-1). DCR: 80%. PFS: 5.7 måneder	
Liu et al.(27)	2021	Single arm, fase 2	2c	Pembrolizumab behandling		36 patienter, bløddelssarkomer	ORR: 19.4% 7/36 patienter PFS: 2.9 måneder (95%CI: 2.4 – 3.4)	Mange forskellige histologiske undergrupper og nogle havde fået pembrolizumab i kombination med anden behandling.
Boye et al.(28)	2021	Single arm, fase 2	2c	Pembrolizumab		12 Osteosarkom patienter	Vel tolereret ingen klinisk gevinst.	
Wagner et al.(29)	2021	Single arm, fase 2	2c	Ipilimumab behandling sammen med nivolumab		16 angiosarkom patienter	ORR: 25% 6 måneders PFS var 38%	Der var i i særdeleshed effekt hos patienter med kutant angiosarkom
Smrke et al.(30)	2021	Single arm, fase 1	2c	Gemcitabine i kombination med pembrolizumab.		13 patienter. 2 med UPS 11 LMS	Bedste respons 9 uger efter start af behandling LMS stabil sygdom for 8/11 patienter UPS partiel respons 2/2. Mediane PFS var 5.1 måned (95%CI: 2-7 måneder)	

PR: Partiel respons som svare til en reduktion i tumor volumen på 30% eller derover.

DCR: Disease control rate som er patienter med partiel respons og stabil sygdom.

UPS: udifferentieret pleomorft sarkom

LMS: leiomyosarkom

DDLPS: dedifferentieret liposarkom

ASPA: alveolær soft part sarkom

CR: komplet respons

SD: stabil sygdom

PFR: progressions fri rate.

Pt: patienter

ORR: objektiv response rate (PR + CR)

ORRxxx: xxx er den behandling som outcome data relaterer til.

M: måneder

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Bilag 10 – Evidenstabel (Små studier med nogen effekt)

DMCG: DSG		Retningslinjens emne/titel: Pallierende kemoterapi og targetere behandling til patienter med bløddelssarkom – små studier med nogen effekt						
Forfatter/ kilde	År	Undersøgelses-type/design	Under-søgelses-kvalitet jf. Oxford	Intervention	Sammenlignings-intervention	Patient-population	Resultater (outcome)	Kommentarer
Garcia del Muro X et al.(1)	2005	Single-arm, fase 2	2B	Temozolomid (alkylerende)	Ingen	STS (49)	ORR 15.5% PFS 2.2 m OS 8.1 m	5 ud af 11 havde uterintleiomyosarkom
Leahy M et al.(2)	2006	Single-arm, fase 2	2B	Brostallicin (alkylerende)	Ingen	STS (43)	ORR 5 % DCR 50% PFS 2.9 m OS 7.7 m	2. linjebehandling
Hartmann JT et al.(3)	2007	Single-arm fase 2	2B	Bendamustin hydrochlorid (aklylerende)	Ingen	STS (36)	ORR 3% DCR 34%	6 ud af 15 patienter med leiomyosarkom havde stabil sygdom
Wagner AJ et al.(4)	2012	Single-arm, fase 2	2B	Tivantinib (MET inhibitor)	Ingen	ASPS (27)	PFS 5.5 m	
Agulnik M et al.(5)	2012	Singelarm, fase 2	2B	Bevacizumab	Ingen	Angiosarkom, epitheloidt hemangioendothelium (32)	ORR 17% DCR 50% PFS 12.4 m	Studier fra kombinationer og fase 3 forsøg kommer senere
Dickson MA et al.(6)	2012	Single-arm, fase 2	2B	CDK4 hæmmer	Ingen	Differentieret og	ORR 3% DCR: 15%	

						dedifferentieret liposarkom(30)	PFS 4.5 m	
George S et al.(7)	2014	Singelarm, fase 2	2B	Letrozol	Ingen	Uterint leiomyosarkom ER og PR pos (27)	PFS 4 m	
Gupta S et al.(8)	2016	Singelarm, fase 2	2C	Amrubicin	Ingen	STS (24)	PFS 5.8 m OS 26 m	
Dickson MA et al.(9)	2016	Singelarm, fase 2	2B	Palbociclib (CDK4 inhibitor)	Ingen	Differentieret og dedifferentieret liposarkom (30)	PFS 4.4 m	Anden tidsperiode
Schöffski P et al.(10)	2017	Singelarm, fase 2	2C	Crizotinib (tyrsin kinase hæmmer)	Ingen	Clear celle sarkom med MET alterationer (27)	ORR 3.8% DCR69.2 % PFS 4.4 m OS 9.2 m	
Tawbi HA et al.(11)	2017	Singelarm, fase 1	2B	Pembrolizumab (immunterapi)	Ingen	STS (40)	ORR 18% UPS (4/10) og dedifferentieret liposakom (2/10)	Dvs. 4 ud af 10 UPS patienter responderede

PR: Partiel respons som svare til en reduktion i tumor volumen på 30% eller derover.

DCR: Disease control rate som er patienter med partiel respons og stabil sygdom.

UPS: udifferentieret pleomorft sarkom

LMS: leiomyosarkom

DDLPS: dedifferentieret liposarkom

ASPA: alveolær soft part sarkom

CR: komplet respons

SD: stabil sygdom

PFR: progressions fri rate.

Pt: patienter

ORR: objektiv response rate (PR + CR)

ORRxxx: xxx er den behandling som outcome data relaterer til.

M: måneder

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Bilag 11 – Evidenstabel (Ingen effekt)

DMCG: DSG	Retningslinjens emne/titel: Pallierende kemoterapi og targeteret behandling til patienter med bløddelssarkom – ingen effekt							
Forfatter/ kilde	År	Undersøgelses-type/design	Under-søgel-sens kvalitet jf. Oxford	Intervention	Sammenlignings intervention	Patient-population	Resultater (outcome)	Kommentarer
Taylor SA et al.(1)	1990	Single-arm, fase 2	2B	Echinomycin (interkalerende peptid)	Ingen	STS (34)	ORR 0%	Ingen effekt
Earhart RH et al.(2)	1990	Randomiseret, fase 2	2B	6-diazo5oxoL norleucine (DON) (glutamin antagonist)	Aclacinomycin A (ACM)	STS (98)	ORRdon 0% OSdon 4.8 m OSacm 6.8 m	Ingen effekt
Muss HB et al.(3)	1990	Single-arm, fase 2	2C	Mitoxantrone (type II topoisomerase hæmmer)	Ingen	Uterint leiomyosarkoma (29)	PFS 1.4 m OS 4.1 m	
Casper ES et al.(4)	1991	Single-arm, fase 2	3	PALA + dipyridamole (phosphodiesterase hæmmer)	Ingen	STS (21)		Ingen effekt
Kerbrat P et al.(5)	1992	Single-arm, fase 2	2C	Fotemustine (alkylerende)	Ingen	STS (31)		Ingen effekt
Somers R et al.(6)	1992	Single-arm, fase 2	2C	Mitozolomide (alkylerende)	Ingen	STS (29)		Ingen effekt
Schiesel JD et al.(7)	1992	Single-arm, fase 2	2C	Piritrexin	Ingen	STS (26)		Ingen effekt
Kraut EH et al.(8)	1992	Single-arm, fase 2	2B	Merbarone (topoisomerase II hæmmer)	Ingen	STS (37)		Ingen effekt

Casper ES et al.(9)	1993	Single-arm, fase 2	2B	Edatrexate	Ingen	STS (35)	ORR 14%	Sparsom effekt fraset ved MFH
Zalupski MM et al.(10)	1993	Single-arm, fase 2	2C	Piroxantrone	Ingen	STS (25)	ORR 9%	Ingen effekt
Borden EC et al.(11)	1993	Single-arm, fase 2	2B	Interferon alfa	Ingen	STS (87)	ORR 5%	Ingen effekt
Verweij J et al.(12)	1994	Single-arm, fase 1	3	MTP/PE	Ingen	STS (20)		Ingen effekt
Knowling M et al.(13)	1994	Single-arm, fase 2	2C	10-EDAM	Ingen	STS (31)		Ingen effekt
Asbury R et al.(14)	1995	Single-arm fase 2	3	Aminothiadiazo le	Ingen	Uterintleiomyo sarkom (21)	ORR 0% DCR 25%	Ingen effekt
Curé H et al.(15)	1998	Single-arm, fase 2	2B	Cystemustine	Ingen	STS (32)	ORR 3.6%	Ingen effekt
Woll PJ et al.(16)	1999	Single-arm, fase 2	2B	Temozolomide (alkylerende)	Ingen	STS (31)	ORR 3.3% PFS 1.8 m OS 6.3 m	Ingen effekt
Blay JY et al.(17)	1999	Single-arm, fase 2	3	Raltitrexed (antimetabolit)	Ingen	STS (23)		Ingen effekt
Smith HO et al.(18)	2002	Single-arm, fase 2		Trimetrexate	Ingen	Uterint leiomyosarkom (28)		Ingen effekt
Kuenen BC et al.(19)	2003	Single-arm, fase 2	2C	SU5416 (tyrosin kinase hæmmer)	Ingen	STS (31)	PFS 2 m	Ingen effekt
Patel SR et al.(20)	2003	Single-arm, fase 2	2B	9- nitrocamptotheci n (topoisomerase hæmmer)	Ingen	STS (56)	ORR 8%	Ingen effekt
Okuno S et al.(21)	2005	Single-arm, fase 2	3	Epothilone B (hæmmer microtubili funktion)	Ingen	STS (21)	PFS 4.5 m OS 16.4 m	Ingen effekt

Bailey HH et al.(22)	2006	Single-arm, fase 2	3	Perifosine (Akt inhibitor og PI3K inhibitor)	Ingen	STS (23)	DCR 9%	Ingen effekt
Patel S et al.(23)	2006	Single-arm, fase 2	2C	TZT-1027	Ingen	STS (29)	PFS 1.5 m OS 5.9 m	Ingen effekt
Reichardt P et al.(24)	2007	Single-arm, fase 2	2B	Exatecan (strukturel analog)	Ingen	STS (39)	DCR 60%	Ingen effekt
Ray-Coquard I et al.(25)	2008	Single-arm, fase 2	2B	Gefitinib (EGFR hæmmer)	Ingen	HER1 synovialt sarkom (48)		Ingen effekt
Baker LH et al.(26)	2009	Single-arm, fase 2	2B	Thrombospindin-1 minetic angiogenesis inhibitor	Ingen	STS (42)	PFS 3.1 m	Ingen effekt
Okuno S et al.(27)	2011	Single-arm fase 2	2B	Temsirolimus (mTOR hæmmer)	Ingen	STS (41)	PFS 2.1	Ingen effekt
Schuetze SM et al.(28)	2012	Randomiseret, fase 2	1B	Sirolimus (makrolid) + cyclophosphamid)	Ingen	STS (49)	PFS 3.4 OS 9.9	Ingen effekt
Ha HT et al.(29)	2013	Single-arm, fase 2	2C	Cetuximab (EGFR hæmmer)	Ingen	STS (21)	PFS 1.7 m OS 7.7 m	Ingen effekt
Cassier PA et al.(30)	2013	Single-arm, fase 2	2B	Panobinostat (histrone deacetylase hæmmer)	Ingen	STS (47)		Ingen effekt
Eroglu Z et al.(31)	2015	Randomiseret, fase 2	2B	Selumetinib (hæmmer af MAPK/ERK)	Selumetinib + temsirolimus	STS (71)		Ingen effekt

				pathway) BRAF mut				
Toulmonde M et al.(32)	2015	Single-arm, fase 2	2B	Aplidin	Ingen	Dedifferentieret liposarkom (24)	PFS 1.6 m OS 9.2 m	Ingen effekt
Schmitt T et al.(33)	2016	Single-arm, fase 2	2B	Vorinostat (histone deacetylase hæmmer)	Ingen	STS (40)	ORR 0% DCR 9% PFS 3.2 m OS 12.3 m	Ingen effekt 2. linjebehandling eller senere
Større studier uden effekt, ikke sammenlignet med tidligere anvendte stoffer.								
Chugh R et al.(35)	2009	Single-arm, fase 2	2A	Imatinib		STS (185)		Ingen effekt
Schuetz SM et al. (36)	2016	Single-arm, fase 2	2A	Dasatinib		STS (200)		Evt. lidt effekt i UPS

PR: Partiel respons som svare til en reduktion i tumor volumen på 30% eller derover.

DCR: Disease control rate som er patienter med partiel respons og stabil sygdom.

UPS: udifferentieret pleomorft sarkom

LMS: leiomyosarkom

DDLPS: dedifferentieret liposarkom

ASPA: alveolær soft part sarkom

CR: komplet respons

SD: stabil sygdom

PFR: progressions fri rate.

Pt: patienter

ORR: objektiv response rate (PR + CR)

ORRxxx: xxx er den behandling som outcome data relaterer til.

M: måneder

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Bilag 12 – Evidenstabel (Review)

DMCG: DSG		Retningslinjens emne/titel: <i>Pallierende kemoterapi og targeteret behandling til patienter med bløddelssarkom - review</i>						
<i>Forfatter/ kilde</i>	<i>År</i>	<i>Undersøgelses-type/design</i>	<i>Under-søgel-sens kvalitet jf. Oxford</i>	<i>Intervention</i>	<i>Sammenlignings intervention</i>	<i>Patient-population</i>	<i>Resultater (outcome)</i>	<i>Kommentarer</i>
<i>Pang A et al.(1)</i>	2016	Review		<i>Pallierende kemoterapi til STS</i>				<i>Generelt anvendt til at sikre at relevant original litteratur er inkluderet i denne retningslinje</i>
<i>Le Cesne A et al.(2)</i>	2015	Review		<i>Trabectedin</i>				<i>Trabectedin kan anvendes ved ældre og flere behandlinger giver ikke mere toksicitet</i>
<i>Radaelli S et al.(3)</i>	2014	Review		<i>Pallierende kemoterapi til STS</i>				<i>Generelt, anvendt til at sikre at relevant original litteratur er inkluderet i denne retningslinje</i>
<i>Jain A et al.(4)</i>	2009	Review		<i>Pallierende kemoterapi til STS</i>				<i>Generelt, anvendt til at sikre at relevant original litteratur er inkluderet i denne retningslinje</i>

Kopp HG et al. (5)	2008	Review		Pallierende kemoterapi til STS				Generelt, anvendt til at sikre at relevant original litteratur er inkluderet i denne retningslinje
Tascilar M et al.(6)	2007	Review		Ifosfamid monoterapi				ORR 16%-55% OS 9-18 m
Sleijfer S et al.(7)	2005	Review		Doxorubicin	Doxorubicin + andre kemoterapeutika			ORR 16-27% OS 7.7 -12 m Begrænsende pga myelosuppression og cardiomyopati
Bauer S et al.(8)	2004	Review		Gemcitabin	Gemcitabin + andre kemoterapeutika			Effektiv ved angiosarkom evt ved LMS non-GI origin
Bramwell VH et al.(9)	2003	Review		Doxorubicin				
Verma S et al. (10)	2008	Review		Ifosfamid				
Fury MG et al.(11)	2005	Retrospektiv		Forskellige behandlinger		Angiosarkom (125)		Doxorubicin (12 pt) PFS 3.7 m Caelyx (11 pt) PFS 4.2 m Paclitaxel (41 pt) 4.0 m Gemcitabin (11 pt) 2.2 m Vinorelbine (6 pt) 3.1 m Ifosfamid (12 pt) 1.6 m

PR: Partiel respons som svare til en reduktion i tumor volumen på 30% eller derover.

DCR: Disease control rate som er patienter med partiel respons og stabil sygdom.

UPS: udifferentieret pleomorft sarkom

LMS: leiomyosarkom

DDLPS: dedifferentieret liposarkom

ASPA: alveolær soft part sarkom

CR: komplet respons

SD: stabil sygdom

PFR: progressions fri rate.

Pt: patienter

ORR: objektiv response rate (PR + CR)

ORRxxx: xxx er den behandling som outcome data relaterer til.

M: måneder

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8. Om denne kliniske retningslinje

Denne kliniske retningslinje er udarbejdet i et samarbejde mellem Danske Multidisciplinære Cancer Grupper (DMCG.dk) og Regionernes Kliniske Kvalitetsudviklingsprogram (RKKP). Indsatsen med retningslinjer er forstærket i forbindelse med Kræftplan IV og har til formål at understøtte en evidensbaseret kræftindsats af høj og ensartet kvalitet i Danmark. Det faglige indhold er udformet og godkendt af den for sygdommen relevante DMCG. Sekretariatet for Kliniske Retningslinjer på Kræftområdet har foretaget en administrativ godkendelse af indholdet. Yderligere information om kliniske retningslinjer på kræftområdet kan findes på:

www.dmcg.dk/kliniske-retningslinjer

Retningslinjen er målrettet klinisk arbejdende sundhedsprofessionelle i det danske sundhedsvæsen og indeholder systematisk udarbejdede udsagn, der kan bruges som beslutningsstøtte af fagpersoner og patienter, når de skal træffe beslutning om passende og korrekt sundhedsfaglig ydelse i specifikke kliniske situationer.

De kliniske retningslinjer på kræftområdet har karakter af faglig rådgivning. Retningslinjerne er ikke juridisk bindende, og det vil altid være det faglige skøn i den konkrete kliniske situation, der er afgørende for beslutningen om passende og korrekt sundhedsfaglig ydelse. Der er ingen garanti for et succesfuldt behandlingsresultat, selvom sundhedspersoner følger anbefalingerne. I visse tilfælde kan en behandlingsmetode med lavere evidensstyrke være at foretrække, fordi den passer bedre til patientens situation.

Retningslinjen indeholder, udover de centrale anbefalinger (kapitel 1), en beskrivelse af grundlaget for anbefalingerne – herunder den tilgrundliggende evidens (kapitel 3+4). Anbefalinger mærket A er stærkest, anbefalinger mærket D er svagest. Yderligere information om styrke- og evidensvurderingen, der er udarbejdet efter "Oxford Centre for Evidence-Based Medicine Levels of Evidence and Grades of Recommendations", findes her: http://www.dmcg.dk/siteassets/kliniske-retningslinjer--skabeloner-og-vejledninger/oxford-levels-of-evidence-2009_dansk.pdf

Generelle oplysninger om bl.a. patientpopulationen (kapitel 2) og retningslinjens tilblivelse (kapitel 5) er også beskrevet i retningslinjen. Se indholdsfortegnelsen for sidehenvvisning til de ønskede kapitler.

For information om Sundhedsstyrelsens kræftpakker – beskrivelse af hele standardpatientforløbet med angivelse af krav til tidspunkter og indhold – se for det relevante sygdomsområde: <https://www.sst.dk/>

Denne retningslinje er udarbejdet med økonomisk støtte fra Sundhedsstyrelsen (Kræftplan IV) og RKKP.