ESMO SARCOMA & GIST

CHALLENGES IN EXPLOITING MEDICAL THERAPIES FOR DESMOID TUMORS

SPAEN & DTRF & EORTC / STBSG

Prof. Dr. med. Bernd Kasper
Mannheim University Medical Center, Mannheim, Germany
on behalf of **The Desmoid Tumor Working Group**

Background

- Desmoid tum
  proliferation c
  unpredictable
- The incidence
  population per
- There was no l
  approach for D
  conducted studie
- Initially, The Des
  Position Paper in
  based on a **joi**
  Roundtable Meeti
  Germany.

* *Kasper B et al. Eur J Cancer 20.*

Annals of Oncology 28: 2399–2408, 2017
doi:10.1093/annonc/mdx323
Published online 23 June 2017

REVIEW

An update on the management of sporadic desmoid-type fibromatosis: a European Consensus Initiative between Sarcoma PAtients EuroNet (SPAEN) and European Organization for Research and Treatment of Cancer (EORTC)/Soft Tissue and Bone Sarcoma Group (STBSG)

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†Additional Members of Desmoid Working Group are listed in the Acknowledgements.

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type fibromatosis:
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Patients EuroNet and
and Treatment of
na Group initiative

Haas[d], F. Haller[e], P. Hohenberger[a],
i[h], on behalf of the Desmoid Working

Sarcoma Patients EuroNet

EORTC
European Organization for Research and Treatment of Cancer

European Reference Network
for rare or low prevalence complex diseases
Network Adult Cancers (ERN EURACAN)

The Desmoid Tumor Working Group went global!

EORTC
European Organization for Research and Treatment of Cancer

18th of June 2018, Istituto Nazionale dei Tumori, Milan, Italy

UMM
UNIVERSITÄTSMEDIZIN MANNHEIM

Sarcoma Patients EuroNet

DTRF
THE DESMOID TUMOR RESEARCH FOUNDATION

sos desmoid

Medizinische Fakultät Mannheim der Universität Heidelberg
Universitätsklinikum Mannheim

Desmoid Meeting 2018 - Topics Covered

- Pathology & Molecular Genetics
- Indications for an Active Treatment incl. Radiotherapy
- ➢ **Available Medical Therapies in Different Indications**
- Assessment of Treatment Effects
- Pain, Quality of Life, Fertility & Pregnancy
- Which Endpoints, Study Designs & Regulatory Requirements do we need for Desmoids?

DTRF THE DESMOID TUMOR RESEARCH FOUNDATION

Sarcoma Patients EuroNet

sos desmoid

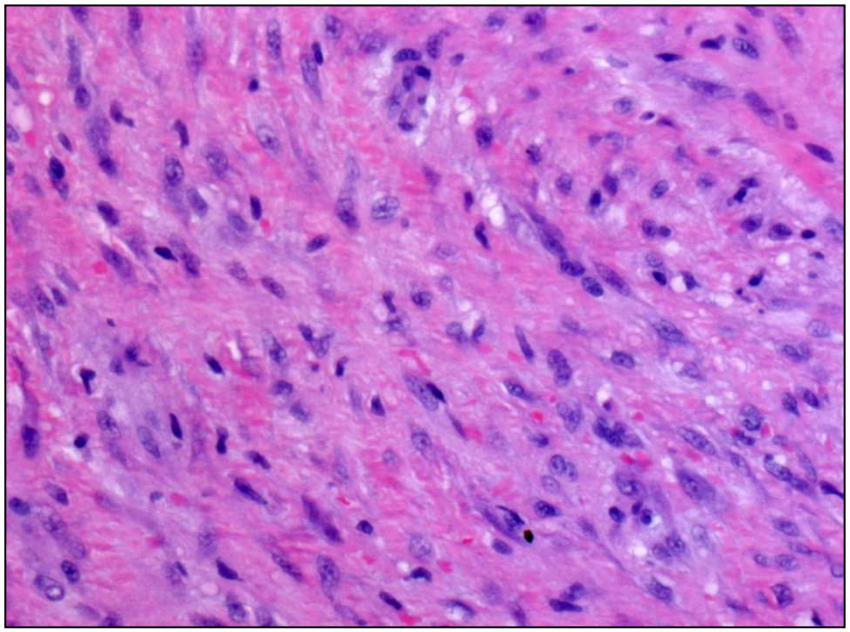
European Reference Network for rare or low prevalence complex diseases

Network Adult Cancers (ERN EURACAN)

EORTC European Organization for Research and Treatment of Cancer

The Systemic Treatment Landscape for Desmoid Tumors

- Active Surveillance
- Surgery
- Radiotherapy
- **Systemic Treatment Options**
  - Antihormonal Therapy (+ NSAID)
  - Chemotherapy
  - Targeted Therapy (TKIs)
  - γ-Secretase Inhibitor Therapy



Kasper B et al. Oncologist 2011; 16: 682-693

Antihormonal Therapy

- Only case reports and small series available[1]
- Response rates vary up to 50 % (bias!)
- No clear rationale available and very low evidence
- Often used in Europe due to easy availability, low costs and rather few side effects!

Indication:	Possible use for progressing, non-resectable DT without or with mild symptoms (preferably in FAP-associated DT[2,3]); BUT no general recommendation

[1] *Janinis J et al. Ann Oncol 2003; 14: 181-190*
[2] *Hansmann A et al. Cancer 2004; 100: 612-620*
[3] *Quast DR et al. Fam Cancer 2016; 15: 31-40*

Antihormonal Therapy

Table 1. Antiestrogen therapy in patients with aggressive fibromatosis: single-arm trials and case reports

Author	No. of patients	Sex	Age, range (median)	History of FAP	Primary or recurrent	Location	Hormonal agent	NSAID	Response	Response duration
Kinzbrunner et al. 1983 [26]	1	F	29	Yes	Recurrent	Multifocal	Tamoxifen 80 mg/day	No	PR	NR
Rock et al. 1984 [27]	5	NR	NR	NR	Recurrent	NR	Tamoxifen	No	2 SD, 3 PD	NR
Procter et al. 1987 [28]	1	F	26	No	Recurrent	Multifocal	Tamoxifen 40 mg/day	No	SD	14 months
Eagel et al. 1989 [29]	1	F	29	Yes	Recurrent	Mesentery	Tamoxifen 20 mg/day, megace 300 mg/day	No	SD	7 months
Sportiello and Hoogerland 1991 [30]	1	F	40	No	Recurrent	Pelvic	Tamoxifen 80 mg/day	No	CR	27 months
Thomas et al. 1990 [31]	1	F	30	No	Recurrent	Shoulder girdle	Tamoxifen 20 mg/day	No	CR	12 months
Wilcken and Tattersall 1991 [32]	2	F	40	No	Recurrent	Calf	Tamoxifen 20 mg/day	No	1 PR	8 years
		F	40	No	Primary	Mesentery	Megace 500 mg/day	No	1 PR	10 months
Brooks et al. 1992 [33]	20	15 F, 5 M	18–70 (29)	NR	12 Primary, 8 recurrent	14 Abdominal and pelvic	Toremifene 200 mg/day	No	1 CR, 10 PR, 6 SD	NR
Benson et al. 1994 [34]	1	F	17	NR	Primary	Retroperitoneum	Toremifene 200 mg/day	No	PR	9 months
Mukherjee et al. 1995 [35]	1	M	16	NR	Primary	Pelvis	Tamoxifen 20 mg/ day, prednisolone 60 mg/day	No	PR	2 years
Izes et al. 1996 [36]	1	M	54	NR	Primary	Pelvis	Tamoxifen 160 mg/day	Sulindac 300 mg/day	PR	54 months
Lackner et al. 1997 [37]	2	F	1	NR	Recurrent	Chest wall	Tamoxifen 2 mg/kg/day	Diclofenac 4 mg/kg/day	SD	4 years
		F	1.5	NR	Primary	Mandible	as above	as above	SD	1 year

CR, complete response; F, female; FAP, familial adenomatous polyposis; M, male; NR, not reported; NSAID, non-steroidal anti-inflammatory agent; PD, progressive disease; PR, partial response; SD, stable disease.

Janinis J et al. Ann Oncol 2003; 14: 181-190

Antihormonal Therapy + NSAID

- Prospective Phase II Study of the Children Oncology Group (COG): **Tamoxifen + Sulindac**
- N = 59 (< 19 years) between 2004 - 2009
- Tamoxifen + Sulindac (each 3 mg/kg/daily) for 12 months
- Only 10 patients completed therapy without PD or withdrawal
- ORR 8 % (5/59)
- 2-years PFS rate 36 % (same as placebo arm in Sorafenib study!)

➢ **First and only prospective study evaluating this combination with rather low activity in terms of overall response and PFS rates**

Skapek SX et al. Pediatr Blood Cancer 2013; 60: 1108-1112

Chemotherapy

- MTX / Vinblastine[1]
- MTX / Vinorelbine[2] or Vinorelbine alone[3]
- Anthracycline-based regimens[4]
- Pegylated liposomal doxorubicin (PLD)[5,6,7]

Indication: Non-resectable, rapidly growing and / or symptomatic or even life-threatening DT should preferably be treated with chemotherapy

[1] *Skapek SX et al. J Clin Oncol 2007; 25: 501-506*
[2] *Palassini E et al. Cancer J 2017; 23: 86-91*
[3] *Mir O et al. J Clin Oncol 2016; 34 (suppl; abstr 11050)*
[4] *De Camargo VP et al. Cancer 2010; 116: 2258-2265*
[5] *Constantinidou A et al. Eur J Cancer 2009; 45: 2930-2934*
[6] *Constantinidou A et al. Acta Oncol 2011; 50: 455-461*
[7] *Pang A et al. J Clin Oncol 2016; 34 (suppl; abstr 11032)*

Chemotherapy

- Prospective Phase II Study of the Paediatric Oncology Group (POG): **MTX + Vinblastine**
- N = 28 (26 evaluable)
- MTX 30 mg/m²/week + Vinblastine 5 mg/m²/week for 26 weeks, every two weeks for an additional 26 weeks (1 year therapy!)
- ORR 19 % (same as placebo arm in the Sorafenib study!)
- Eight patients remain free of PD at a median of 43.4 months from study entry

- **Combination of MTX + Vinblastine demonstrated progression arrest in 1/3 of children**
- **Chemotherapy regimen of choice in the paediatric patient population**

Skapek SX et al. J Clin Oncol 2007; 25: 501-506

Chemotherapy (selected regimens)

Reference	Chemotherapy regimen	Number of patients	Response	Follow-up [months]
Patel	Doxorubicin 60-90 mg/m² + dacarbazine 750-1000 mg/m²	12	2 CR 4 PR 2 SD	28-235
Gega	Doxorubicin 20 mg/m² d1-4 + dacarbazine 150 mg d1-4, d28	7	3 CR 4 PR	33-108
Constantinidou	Pegylated liposomal doxorubicin 50 mg/m², d28	12	4 PR 7 SD	7-39
Wehl	Pegylated liposomal doxorubicin 50 mg/m², d28	4	4 PR	NR
Azzarelli	Vinblastine 6 mg/m² + methotrexate 30 mg/m², weekly	27	4 OR 19 SD	6-96
Weiss	Vinorelbine 20 mg/m² + methotrexate 50 mg/m², weekly	13	NR	< 12
Skapek	Vinblastine 5 mg/m² + methotrexate 30 mg/m², weekly	27	8 PR 10 SD	5-37
Pilz	VAIA, VAC, cyclophosphamide + ifosfamide	19	4 CR 5 PR	NR

No randomized studies!

Kasper B et al. Oncologist 2011; 16: 682-693

Chemotherapy

- Retrospective Analy
- N = 62 (12 pts. with
- Chemotherapies:

Protocol	Drugs
Mesna, adriamycin, ifosfamide, dacarbazine	Doxorubicin 20 mg/m^2 (day 1–day 3) Ifosfamide 2.5 g/m^2 (day 1–day 3) Dacarbazine 300 mg/m^2 (day 1–day 3) 21 days cycle
Adriamycin, dacarbazine	Doxorubicin 20 mg/m^2 (day 1–day 3) Dacarbazine 300 mg/m^2 (day 1–day 3) 21 days cycle
Metronomic etoposide	Oral etoposide 75 mg/day for 21 days of 28 days cycle
Metronomic cyclophospamide	Oral cyclophosphamide 50 mg/day for 21 days of 28 days cycle
Doxorubicin	Doxorubicin 60–75 mg/m^2 21 days cycle
Methotrexate–vinblastine	Vinblastine 6 mg/m^2 Methotrexate 30 mg/m^2 (J1, J8, 15, 21) 28 days cycle
Methotrexate	Methotrexate 30 mg/m2 (J1, J8, 15, 21) 28 days cycle
Vinorelbine	Vinorelbine 20 mg/m^2 (J1, J8) 21 days cycle

- Responses: % PD

- **Response rate high % *vs* 12 %, *p = 0.0011*)**
- **If Chemo is indicate cline-based regimens**
- **PLD may be preferr less cardiac toxicity**

Garbay D et al. Ann Oncol 2012; 23: 182-186

Targeted Therapies: It has all started with Imatinib …

- US Phase II Study (n = 19) with **800 mg Imatinib** daily[1]:
  - ORR 16 % (3 PR and 4 SD)
  - No mutations of KIT, PDGFRA or PDGFRB

- French Sarcoma Group Phase II Study (n = 35) with **400 mg Imatinib** daily[2]:
  - ORR 11 % (1 CR, 3 PR and 28 SD)
  - Progression arrest rates after 3, 6 and 12 months 91 %, 80 % and 67 %
  - 2-year PFS rate 55 % and OS rate 95 %

[1] *Heinrich MC et al. J Clin Oncol 2006; 24: 1195-1203*
[2] *Penel N et al. Ann Oncol 2011; 22: 452-457*

Imatinib induces sustained progression arrest in RECIST progressive desmoid tumors - Final results of a phase II study of the German Interdisciplinary Sarcoma Group (GISG-01)

Bernd Kasper[1], Viktor Grünwald[2], Peter Reichardt[3], Sebastian Bauer[4], Michaela Sommer[1], Geraldine Rauch[5], Florian Haller[6], Peter Hohenberger[1]

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Kasper B et al. Ann Surg Oncol 2016; 23: 1924-1927
Kasper B et al. Eur J Cancer 2017; 76: 60-67

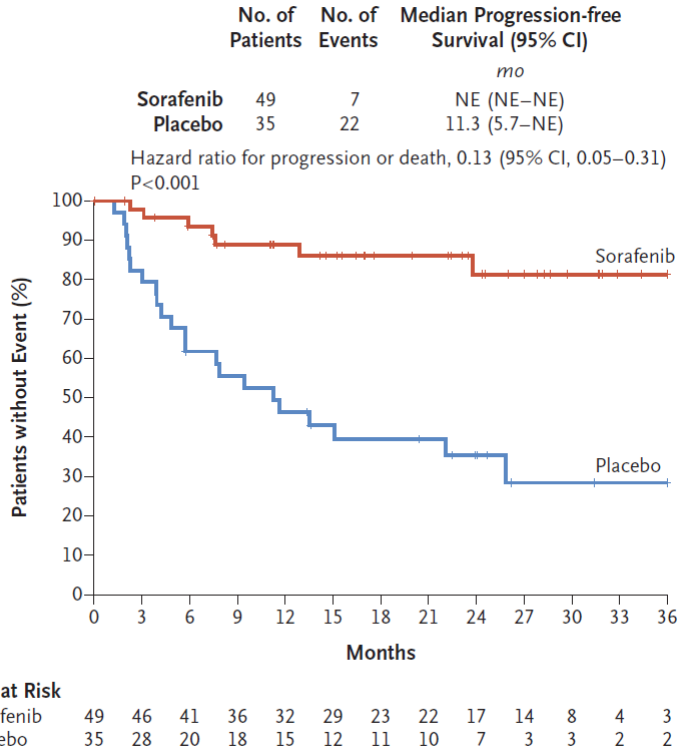
Targeted Therapies: Sorafenib (Alliance A091105)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Sorafenib for Advanced and Refractory Desmoid Tumors

Mrinal M. Gounder, M.D., Michelle R. Mahoney, M.S., Brian A. Van Tine, M.D., Ph.D., Vinod Ravi, M.D., Steven Attia, D.O., Hari A. Deshpande, M.D., Abha A. Gupta, M.D., Mohammed M. Milhem, M.D., Robert M. Conry, M.D., Sujana Movva, M.D., Michael J. Pishvaian, M.D., Ph.D., Richard F. Riedel, M.D., Tarek Sabagh, M.D., William D. Tap, M.D., Natally Horvat, M.D., Ethan Basch, M.D., Lawrence H. Schwartz, M.D., Robert G. Maki, M.D., Ph.D., Narasimhan P. Agaram, M.B., B.S., Robert A. Lefkowitz, M.D., Yousef Mazaheri, Ph.D., Rikiya Yamashita, M.D., Ph.D., John J. Wright, M.D., Ph.D., Amylou C. Dueck, Ph.D., and Gary K. Schwartz, M.D.



Gounder MM et al. N Engl J Med 2018; 379: 2417-2428

Targeted Therapies: Pazopanib (DESMOPAZ)

Pazopanib or methotrexate–vinblastine combination chemotherapy in adult patients with progressive desmoid tumours (DESMOPAZ): a non-comparative, randomised, open-label, multicentre, phase 2 study

Maud Toulmonde, Marina Pulido, Isabelle Ray-Coquard, Thierry Andre, Nicolas Isambert, Christine Chevreau, Nicolas Penel, Emmanuelle Bompas, Esma Saada, François Bertucci, Celeste Lebbe, Axel Le Cesne, Patrick Soulie, Sophie Piperno-Neumann, Stephen Sweet, Fabiola Cecchi, Todd Hembrough, Carine Bellera, Michèle Kind, Amandine Crombe, Carlo Lucchesi, François Le Loarer, Jean-Yves Blay, Antoine Italiano

Summary

Background Desmoid tumours are locally aggressive tumours associated with substantial morbidity. No systemic treatments are approved for this disease, with methotrexate–vinblastine the only chemotherapy regimen assessed in a clinical trial setting to date. VEGF overexpression is a common feature in aggressive desmoid tumours. Pazopanib is an oral antiangiogenic agent targeting VEGF receptors 1, 2, and 3, platelet-derived growth factor receptor-like protein (PDGFR) α and β, and c-KIT tyrosine kinases. We aimed to assess antitumour activity and safety of targeted therapy or combination chemotherapy in progressive desmoid tumours.

Methods DESMOPAZ was a non-comparative, randomised, open-label, phase 2 trial conducted at 12 centres from the French Sarcoma Group. We enrolled adults (≥18 years) with progressive desmoid tumours, normal organ function and centrally documented progressive disease according to Response Evaluation Criteria in Solid Tumors version 1.1 based on two imaging assessments obtained within less than a 6-month interval. Participants were randomly assigned (2:1) to oral pazopanib 800 mg per day for up to 1 year or to an intravenous regimen combining vinblastine (5 mg/m² per dose) and methotrexate (30 mg/m² per dose), administered weekly for 6 months and then every other week for 6 months. Randomisation was stratified according to inclusion centre and tumour location. The primary endpoint was the proportion of patients who had not progressed at 6 months in the first 43 patients who had received one complete or two incomplete cycles of pazopanib. This endpoint was also assessed as a prespecified exploratory endpoint in all patients who had received one complete or two incomplete cycles of methotrexate–vinblastane. Safety analyses were done for all patients who received at least one dose of allocated treatment. This trial was registered with ClinicalTrials.gov, number NCT01876082.

Findings From Dec 4, 2012, to Aug 18, 2017, 72 patients were enrolled and randomly assigned (n=48 in the pazopanib group; n=24 in the methotrexate–vinblastine group). Median follow-up was 23·4 months (IQR 17·1–25·5). 46 patients in the pazopanib group and 20 patients in the methotrexate–vinblastine group were assessable for activity. In the first 43 patients assessable for the primary endpoint in the pazopanib group, the proportion of patients who had not progressed at 6 months was 83·7% (95% CI 69·3–93·2). The proportion of patients treated with methotrexate–vinblastine who had not progressed at 6 months was 45·0% (95% CI 23·1–68·5). The most common grade 3 or 4 adverse events in the pazopanib group were hypertension (n=10, 21%) and diarrhoea (n=7, 15%) and in the methotrexate–vinblastine group were neutropenia (n=10, 45%) and liver transaminitis (n=4, 18%). 11 patients (23%) had at least one serious adverse event related to study treatment in the pazopanib group, as did and six patients (27%) in the methotrexate–vinblastine group.

Interpretation Pazopanib has clinical activity in patients with progressive desmoid tumours and could be a valid treatment option in this rare and disabling disease.

Lancet Oncol 2019

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See Online/Comment http://dx.doi.org/10.1016/S1470-2045(19)30323-7

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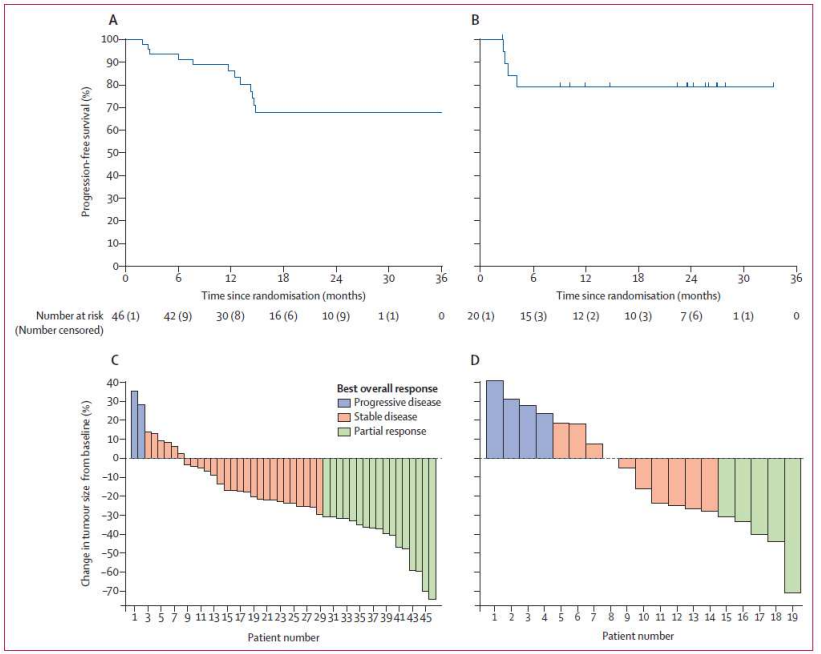


Figure 2: **Overall response and progression-free survival**
(A) Progression-free survival in the pazopanib group (n=46). (B) Progression-free survival in the methotrexate–vinblastine group (n=20). (C) Best overall response of 46 patients included in the pazopanib group. (D) Best overall response of 19 patients included in the methotrexate-vinblastine group (one patient had no radiological assessment available).

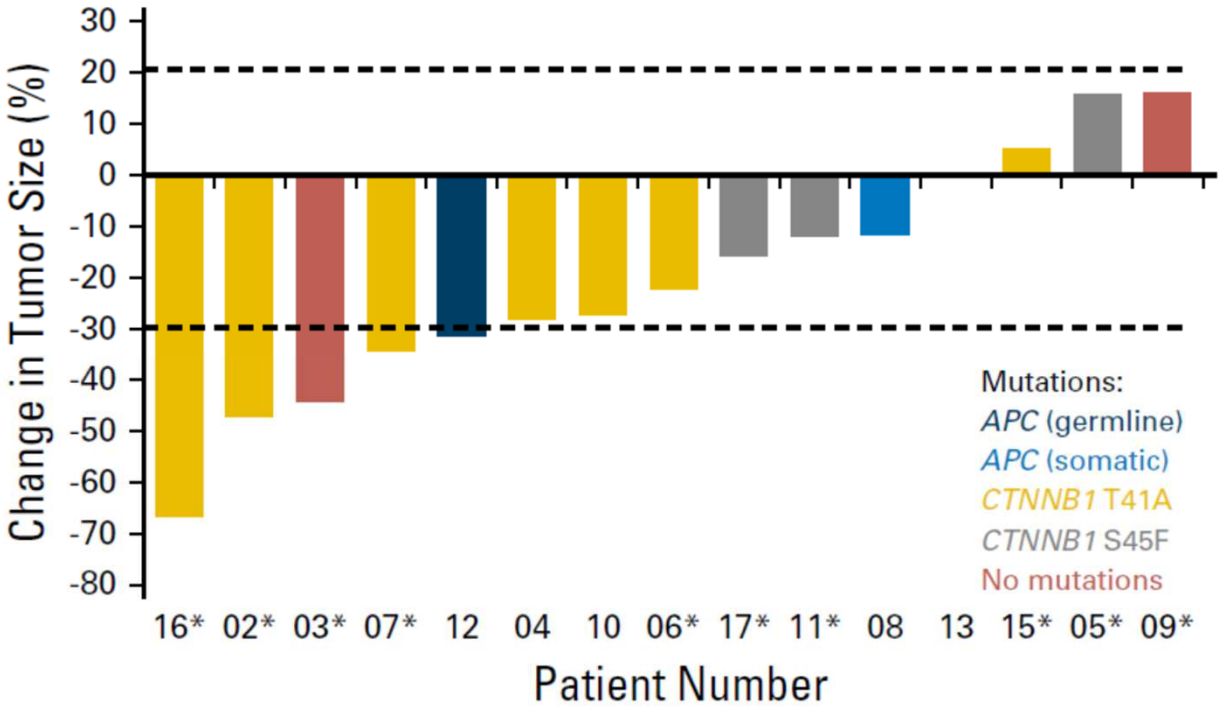
Toulmonde M et al. Lancet Oncol 2019; Jul 19 pii: S1470-2045

γ-Secretase Inhibitor (GSI): Nirogacestat (Phase II)

Patient Characteristics (N=17)	No.*
Median Age, (range), Years	34 (19-69)
Gender	
Male	3 (18)
Female	14 (82)
Primary Tumor Site	
Thorax	1 (6)
Abdomen	4 (24)
Extremity	6 (35)
Spine + Spinal Girdles	6 (35)
ECOG Performance Status	
0	1 (6)
1	16 (94)
Median No. of Prior Therapies, No. (range)	4 (1-9)
Cytotoxic chemotherapy†	12 (71)
NSAID (sulindac, celecoxib)	11 (65)
TKI (imatinib, sorafenib)	10 (59)

Kummar S et al. J Clin Oncol 2017; 35: 1561-1569

γ-Secretase Inhibitor (GSI): Nirogacestat (Phase II)



Kummar S et al. J Clin Oncol 2017; 35: 1561-1569

γ-Secretase Inhibitor (GSI): Nirogacestat (Phase II)

Adverse Events (N=17)	Grade 1 No. %	Grade 2 No. %	Grade 3 No. %
Anemia	6 (35)		
Diarrhea	10 (59)	3 (18)	0
Dry Mouth	7 (41)	0	0
Mucositis Oral	3 (18)	1 (6)	
Nausea	9 (53)	0	0
Fatigue	7 (41)	0	0
ALT Elevated	5 (29)	1 (6)	0
AST Elevated	10 (59)	0	0
Lymphocyte Count Decreased	8 (47)	1 (6)	0
Platelet Count Decreased	4 (24)		
White Blood Cell Count Decreased	3 (18)	1 (6)	
Hypocalcemia	5 (29)		
Hypokalemia	4 (24)		
Hyponatremia	4 (24)		
Hypophoshatemia		5 (29)	8 (47)
Irregular Menstruation	4 (24)		
Rash (maculopapular)	5 (29)	4 (24)	0
Hot Flashes	5 (29)		

Kummar S et al. J Clin Oncol 2017; 35: 1561-1569

γ-Secretase Inhibitor (GSI): Nirogacestat (Phase III)

γ-Secretase Inhibitor (GSI): Nirogacestat (Phase III)

Study Design

- Global, randomized, double-blind, placebo-controlled, phase 3 trial evaluating the efficacy, safety, and tolerability of nirogacestat in adult patients with progressing DTs/AF[1,2]
  - Estimated primary completion: March 31, 2021[3]
  - Estimated study completion: March 31, 2023[3]

Eligible Patients[2]

Participant has:

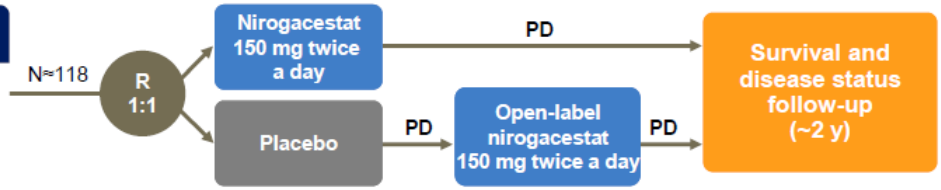
- Treatment-naïve measurably progressing DT/AF deemed not amenable to surgery without the risk of significant morbidity

OR

- Recurrent, measurably progressing DT/AF following at least one line of therapy

OR

- Refractory, measurably progressing DT/AF following at least one line of therapy



End Points[2]

Primary

- Progression-free survival

Secondary

- Safety, ORR, DOR, volumetric tumor change by MRI, PRO

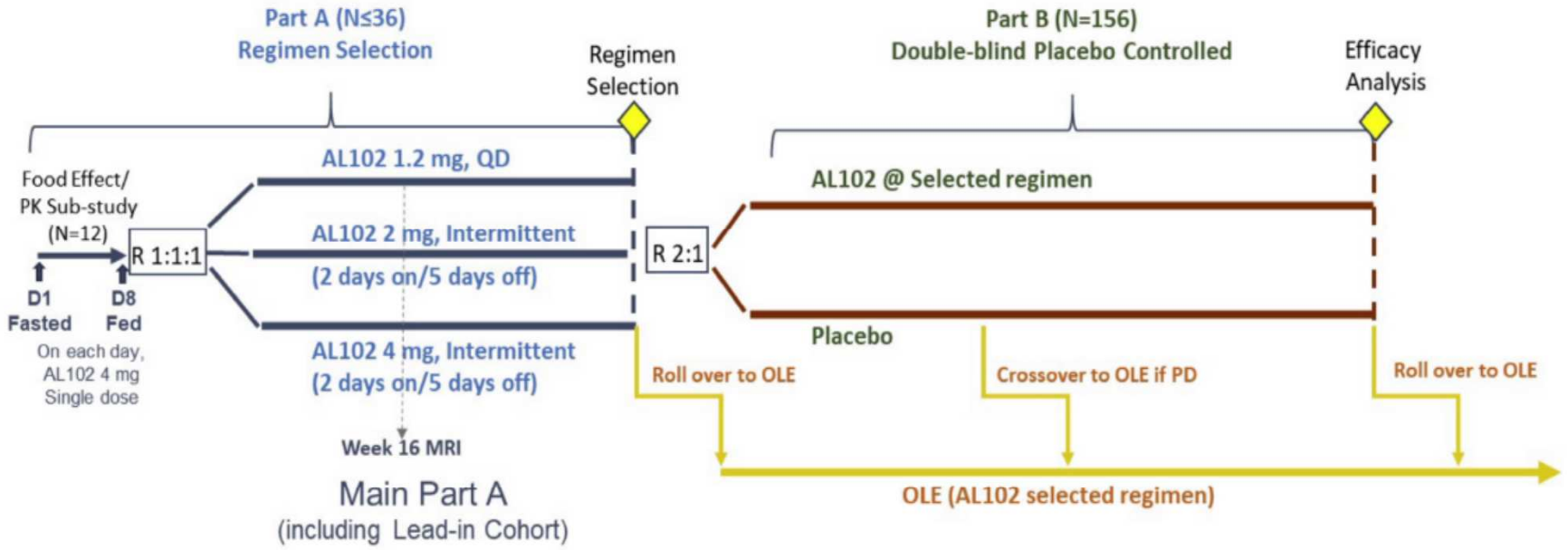
- DeFi trial: First patient dosed May 20, 2019[1]

AF, aggressive fibromatosis; CR, complete response; DeFi, desmoid fibromatosis trial; DOR, duration of response; DTs, desmoid tumors; MRI, magnetic resonance imaging; ORR, overall response rate; PD, progressive disease; PRO, patient-reported outcome; R, randomized.

1. SpringWorks Therapeutics announces initiation of phase 3 trial (DeFi) of nirogacestat in adult patients with desmoid tumors [press release]. Stamford, CT: SpringWorks Therapeutics; May 20, 2019. https://www.springworkstx.com/wp-content/uploads/2019/05/DeFi-Study-Initiation-Press-Release.pdf. Accessed October 23, 2019. **2.** Nirogacestat for adults with desmoid tumor/aggressive fibromatosis (DT/AF) (DeFi) clinical trial protocol. SpringWorks Therapeutics Inc. **3.** NCT03785964. ClinicalTrials.gov website. https://clinicaltrials.gov/ct2/show/NCT03785964. Updated November 20, 2019. Accessed November 20, 2019.

DeFi

γ-Secretase Inhibitor (GSI): AL102 (Phase II/III)



Abbreviations: CT, computed tomography; D, day; MRI, magnetic resonance imaging; OLE, open-label extension; PK, pharmacokinetics; QD, once daily; R, randomization

ayala pharmaceuticals

Efficacy Summary: TKIs & GSI

	n	Inclusion Criteria	Treatment Dose [mg]	Treatment Duration	ORR [%]	6-month-PFS [%]	12-month-PFS [%]	24-month-PFS [%]
Heinrich et al. *J Clin Oncol 2006*	19	"heavily pretreated patients"	Imatinib 800 mg	325 days	16	53	37	n.e.
Penel et al. *Ann Oncol 2010*	35	"radiological evidence for PD"	Imatinib 400 mg	1 year	11	80	67	55
Chugh et al. *Clin Cancer Res 2010*	49	"locally advanced disease"	Imatinib 200-600 mg	until PD 9 pts. > 3 years	6	84	66	n.e.
Kasper et al. *Eur J Cancer 2017*	38	**RECIST PD**	Imatinib 800 mg	2 years	19	65	59	45
Gounder et al. *NEJM 2018*	50	"progressive or symptomatic"	Sorafenib 400 mg	until PD	33	n.e.	89	81
Toulmonde et al. *Lancet Oncol 2019*	48	**RECIST PD**	Pazopanib 800 mg	1 year	37	84	86	67
Kummar et al. *J Clin Oncol 2017*	17	"progressive / symptomatic"	Nirogacestat 300 mg	until PD	29	100	100	100

Medical Treatment Options for DT - Summary

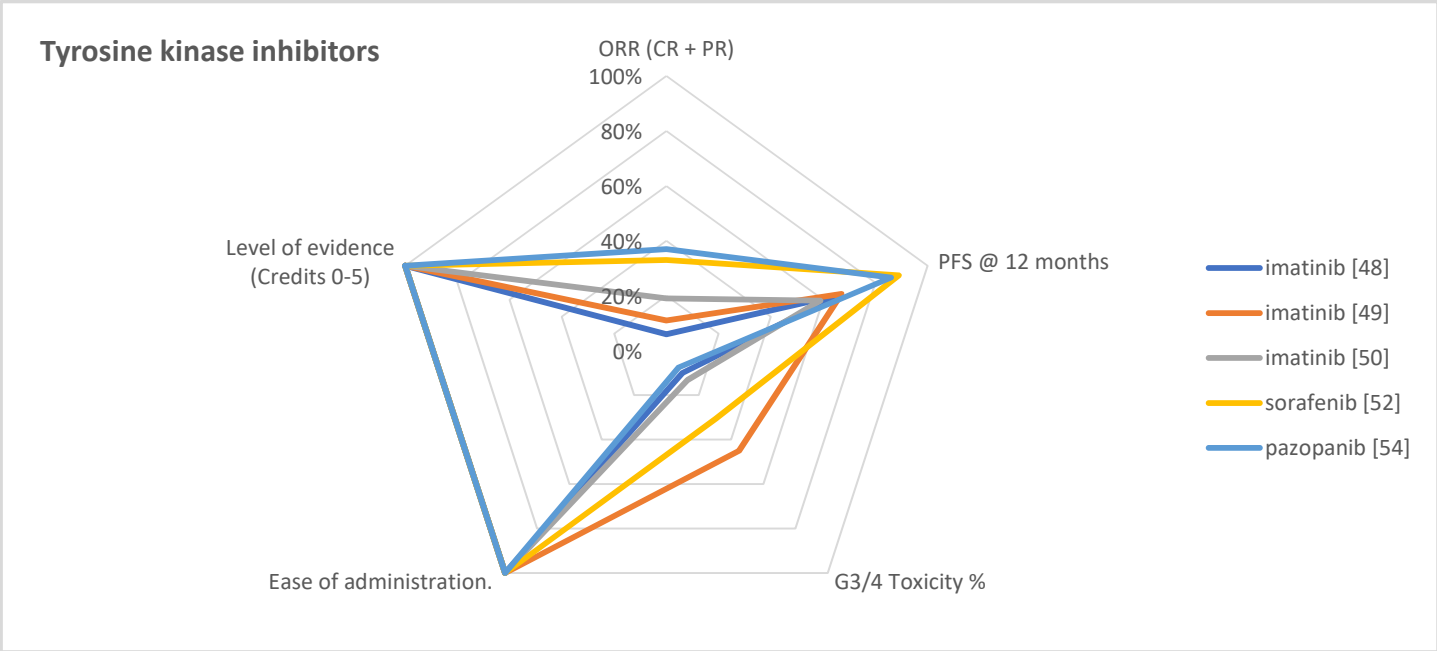
- No recommendation for **Antihormonal Therapies** (+ NSAIDs)
- **Chemotherapy** may be indicated in rapidly growing and/or symptomatic or even life-threatening DT
  - MTX + Vinblastine is the chemotherapy of choice in the paediatric patient population
  - For young (AYA) patients, pegylated liposomal doxorubicin may be preferred
- **TKIs** (sorafenib, pazopanib) clearly demonstrated clinical activity in randomized settings and move into the focus of interest
- **GSIs** promise to be effective agents: Nirogacestat + AL102 studies ongoing

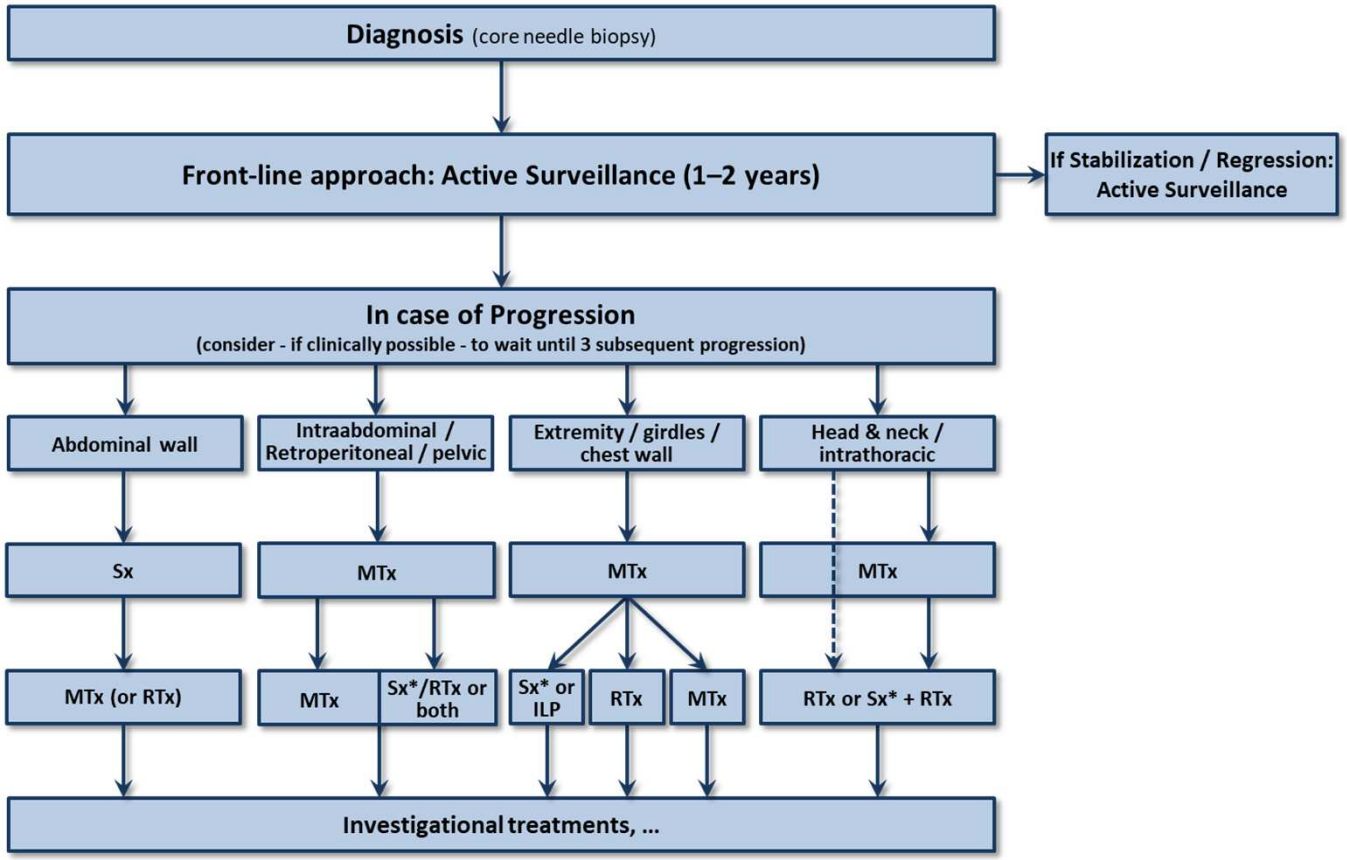
CAVE: Majority of mentioned drugs do not have a formal registration for DT and, therefore, are not available or reimbursed in many European countries!

Desmoid Global Consensus - Available Medical Therapies

- Due to the lack of comparative studies we are still not able to propose a definitive sequence of the existing systemic treatment options.
- Randomized data only exist for sorafenib, pazopanib and methotrexate plus vinblastine.
- Prospective phase II studies do exist for the administration of low-dose chemotherapy with methotrexate plus vinblastine and for the use of imatinib.
- In general, it is reasonable to employ less toxic therapy initially followed by more toxic agents in a stepwise fashion.
- Out of the variety of possible systemic treatment options, one can be chosen taking into account the (1) level of evidence, the (2) overall response rate, the (3) PFS rate, the (4) ease of administration, and the (5) expected toxicity of the administered drug following a 5-dimensional model.

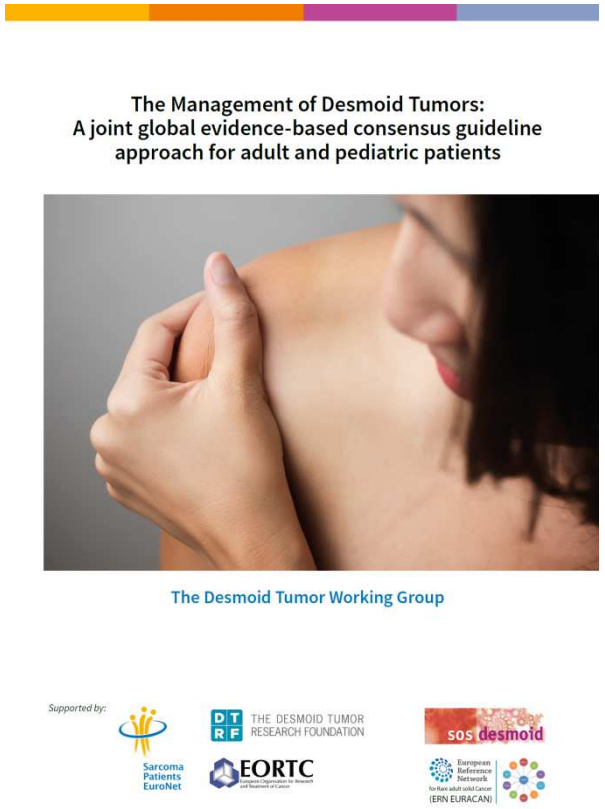
Desmoid Global Consensus - Available Medical Therapies



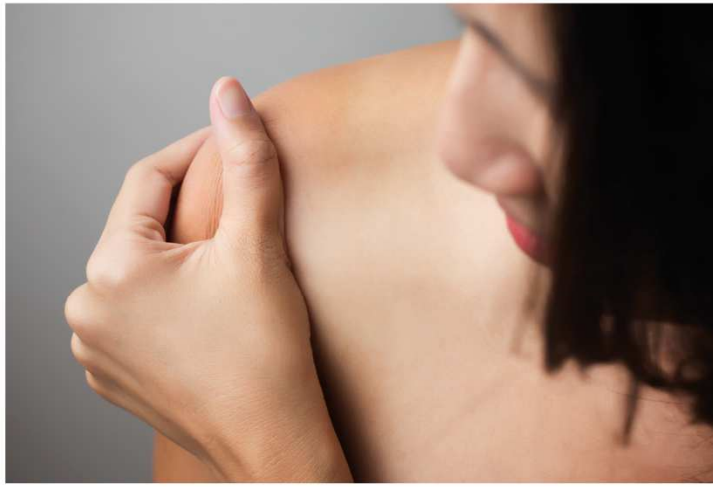


Abbreviations: Sx: Surgery; Sx*: Surgery is an option if morbidity is limited; MTx: Medical treatment; RTx: Radiotherapy; ILP: Isolated limb perfusion.

Desmoid Global Consensus - Publications



The Management of Desmoid Tumors: A joint global evidence-based consensus guideline approach for adult and pediatric patients



The Desmoid Tumor Working Group

Supported by:

Sarcoma Patients EuroNet

THE DESMOID TUMOR RESEARCH FOUNDATION

EORTC European Organisation for Research and Treatment of Cancer

sos desmoid

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