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Supplementary Material

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Table i. An overview of the available evidence regarding different treatments for desmoid tumours: active surveillance.

Study	Patients, n	Period	Inclusion criteria	Type of treatment, n (%)	Median follow-up, mths	PFS, %	Tumour progression (RECIST), n (%)	Tumour regression (RECIST), n (%)	Incidence of treatment initiation/ change, n (%)	Median time to treatment initiation/change
Active surveillance										
Colombo et al 2022[1]	108	2013 to 2018	Primary sporadic DF at any site	AS 108 (100.0)	32.3	54.5 (3 yrs)	42 (39.0)	60 (56.0)	35 (32.0)	7 m
Schut et al 2023[2]	105	2014 to 2018	Non- intra-abdominal DTF	AS 105 (100.0)	33.7	58.0 (3 yrs)	42 (40.0)	29 (28.0)	31 (30.0)	NE
Active surveillance and other treatments										
Bonvalot et al 2008[3]	112	1988 to 2003	Extra-abdominal primary fibromatosis	Surg ± RT 89 (79.5)	76.1	NE	NE	44.0 (3 yrs)	NE	NE
				AS/MT 23 (20.5)	75.6	NE	9/23 (39.0)	68.0 (3 yrs)	NE	NE

Fiore et al 2009[4]	142	1995 to 2008	Primary and recurrent DF	AS 83 (58.5)	33.0	49.9 (5 yrs)	29/83 (35.0)	NE	NE	NE
				MT 59 (41.5)		58.6 (5 yrs)	26/59 (44.0)			
Colombo et al 2015[5]	216	1992 to 2012	Primary sporadic extra-abdominal wall DF	Surg 94 (43.0)	76.0	NE	NE	NE	NE	NE
				Non-surg 122 (57.0)	39.0		53/122 (43)		53/122 (43.0)	13 m
Penel et al 2017[6]	771	2010 to 2016	Primary desmoid-type fibromatosis	Surg: 359 (46.5)	32.0	NE	NE	53.0 (2 yrs) 52.0* (2 yrs)	NE	NE
				Non-surg: 393 (51.0) AS: 388 (50.0) MT/RT 5 (1.0) Unknown 19 (2.5)				58.0 (2 yrs) 25.0* (2 yrs)	71/388 (18.3)	

*Considering patients with unfavorable locations.

AS, active surveillance; DF, desmoid fibromatosis; DTF, desmoid-type fibromatosis; EFS, event-free survival; FU, follow-up; MT, medical treatment; NE, not evaluated; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumor; RT, radiotherapy; surg, surgery.

Table ii. An overview of the available evidence regarding different treatments for desmoid tumours: medical therapies.

Study	Patients, n	Period	Inclusion criteria	Type of treatment, n (%)	Median follow-up, mths	PFS, %	RECIST response, n (%)	ORR, %	Median treatment duration - Median number of cycles	Toxicity (CTCAE), n (%)
Chemotherapy										
Constantinidou et al 2009[7]	12	2006 to 2009	Progressive or recurrent AF	PLD 12 (100)	NE	NE	PR 4/11 (36.0) SD 7/11 (64.0)	36.0	6 cycles	Palmar-plantar erythema G3/G2 4 (33.3) Mucositis G2 3 (25.0)
Garbay et al 2012[8]	62	1993 to 2010	Recurrent and/or unresectable DTs	ANT 13 (21.0) MTX/VBL 27 (43.5) MTX 7 (11.3) ETO/CP 4 (6.5) NVB 6 (9.7) Others 5 (8.1)	71.3	40.8 mths	CR 1 (1.6) PR 12 (19.4) SD 37 (59.6) PD 12 (19.4)	54.0 (ANT) 12.0 (non-ANT)	10 wks (ANT) 18 wks (non-ANT)	Hematological G3/G4 19 (31.0) (ANT) Hematological G3/G4 6 (10.0) (non-ANT)
Palassini et al 2017[9]	75	1989 to 2014	Sporadic desmoid-type fibromatosis	MTX/VBL 30 (40.0) MTX/NVB 43 (57.3) NVB 2 (2.7)	79.4	75.2 mths	CR 1 (1.3) PR 35 (46.7) SD 38 (50.7) PD 1 (1.3)	48.0	13.9 mths 37.5 cycles	G3/G4 8 (10.7) 4/30 (13.3) (MTX/VBL) 4/43 (9.3)

										(MTX/NVB)
Li et al 2017[10]	71	2008 to 2016	Inoperable desmoid tumour	MTX/NVB 71 (100.0)	28	68.4 (3 yrs) 36.3 (5 yrs)	CR 1 (1.4) PR 24 (33.8) SD 37 (52.1) PD 9 (12.7)	87.3	< 12 mths 14/71 (19.7%) > 12 mths 57/71 (80.3%)	NE
Mir et al 2020[11]	90	2009 to 2019	Particularly aggressive forms of DF	NVB 56 (62.0) NVB + endocrine therapy 34 (38.0)	52.4	88.7 (6 mths) 77.5 (12 mths)	PR 26 (29.0) SD 51 (57.0) PD 13 (14.0)	86.0	6.7 mths	Neutropenia G3 1 (1.1)
Tyrosine-kinase/vascular endothelial growth factor inhibitors										
Heinrich et al 2006[12]	19	NE	Heavily pretreated patients	Imatinib (800 mg) 19 (100.0)	NE	53.0 (6 mths) 37.0 (1 yrs)	PR 3 (16.0) SD 13(68.0) PD 3 (16.0)	16.0	325 days	Gastrointestinal 9 (47.0) Dermatologic 3 (16.0) Hematologic 2 (11.0)
Chugh et al 2010[13]	51	2002 to 2005	Locally advanced disease	Imatinib (200-600 mg) 51 (100.0)	NE	94.0 (2 mths) 88.0 (4 mths) 66.0 (1 yrs)	PR 3 (6.0) SD 43 (84.0) PD 5(10.0)	6.0	Until PD	G4/G3 > 5.0
Penel et al 2011[14]	40	2004 to 2005	Unresectable and progressive symptomatic AF/DT	Imatinib (400 mg) 40 (100.0)	34	67.0 (1 yrs) 55.0 (2 yrs)	CR 1 (3.0) PR 3 (8.5) SD 28 (80.0) PD 3 (8.5)	11.5	12 mths	G4 0 G3 18 (45.0)

Kasper et al 2017[15]	38	2010 to 2013	Patients being RECIST progressive, not amenable to surgical resection	Imatinib (800 mg) 38 (100.0)	NE	59.0 (1 yrs) 45.0 (2 yrs)	PR 7 (19.0) SD 7 (19.0) PD 17 (43.0) Missing 7 (19.0)	19.0	2 yrs	G4 1 (3.0) G3 4 (11.0)
Gounder et al 2018[16]	87	2014 to 2016	Progressive, symptomatic, or recurrent desmoid tumours	Sorafenib (400 mg) 50 (57.5)	27.2	81.0 (2 yrs)	CR 1 (2.0) PR 15 (31.0)	33.0	Until PD	G3/G4 23 (47.0)
				Placebo 37 (42.5)		36.0 (2 yrs)	PR 7 (20.0)	20.0	NE	G3/G4 9 (25.0)
Toulmonde et al 2019[17]	72	2012 to 2017	Progressive desmoid tumours	Pazopanib (800 mg) 48 (67.0)	23.4	85.6 (1 yrs) 67.2 (2 yrs)	PR 17 (37·0) SD 27 (58·7) PD 2 (4·4)	37.0	1 yr	G3/G4 27 (56.0)
				MTX (30 mg/m^2)/VBL (5 mg/m^2) 24 (33.0)		79.0 (1 yrs) 79.0 (2 yrs)	PR 5 (25.0) SD 10 (50.0) PD 4 (20.0)	25.0	1 yr	G3/G4 17 (77.0)
Nirogacestat (PF-03084014), a gamma-secretase inhibitor										
Kummar et al 2017[18]	17	NE	Recurrent, refractory, progressive desmoid tumours	PF-03084014 (150 mg twice daily) 17 (100.0)	>25	100.0 (2 yrs)	CR 0 (0) PR 5 (29.0) SD 11 (65.0) DP 0 (0) Not evaluated 1 (6.0)	29.0	36 cycles	G1/G2 17 (100.0) G3 8 (47.0) G 4 0 (0)

Villalobos et al 2017[19]	7	2009 to 2016	Desmoid fibromatosis	PF-03084014 (20 - 330 mg twice daily) 7 (100.0)	NE	NE	PR 5 (71.4) SD 1 (14.3) PD 1 (14.3)	71.4	49.5 mths	Diarrhoea (55.0) Nausea (38.0) Fatigue (30.0) Hypophosphatemia (27.0) Vomiting (23.0)
Gounder et al 2023[20]	142	2019 to 2022	Progressing DT per RECIST v1.1	PF-03084014 (150 mg) 70 (49.3)	19.2	Median NE	CR 5 (7.0) PR 24 (34.0) SD 35 (50.0) PD 1 (1.0) NE 4 (6.0)	41.0	20.6 mths	Any grade 69 (100.0) G3/G4 39 (57.0)
				Placebo 72 (50.7)	10.9	Median 15.1 m	CR 0 (0) PR 6 (8.0) SD 55 (76.0) PD 10 (14.0) NE 1 (1.0)	8.3	11.4 mths	Any grade 69 (96.0) G3/G4 12 (17.0)

*Considering 35 patients in whom central radiological review of the three-month response rate was possible.
AF, aggressive fibromatosis; ANT, anthracycline; CR, complete response; CTCAE, Common Terminology Criteria for Adverse Events; CP, cyclophosphamide; DF, desmoid fibromatosis; DT, desmoid tumor; ETO, etoposide; FU, follow-up; MTX, methotrexate; NE, not evaluated; NVB, vinorelbine; ORR, objective response rate; PD, progressive disease; PLD, pegylated liposomal doxorubicin; PFS, progression-free survival; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumor; SD, stable disease; VBL, vinblastine.

Table iii. An overview of the available evidence regarding different treatments for desmoid tumours: local treatments.

Radiotherapy											
Author, year	**Patients, n**	**Period**	**Inclusion criteria**	**Type of treatment (dose), n (%)**	**Media n follow-up, mths**	**OS, %**	**RECIST response, n (%)**	**Local control, %**	**LR n (%)**	**Median time to LR, mths**	**Toxicity n (%)**
Bishop et al 2018[21]	209	1965 to 2015	Consecutive patients with histologically confirmed non mesenteric desmoid soft-tissue tumours	RT alone 56 Gy (50 to 75): 121 (58.0)	78	5-yr: 99.0 10-yr: 93.0	NE	< 30 years old, 5-yr: 43.0	59 (28.0)	23	32 (15.0) Mild: 8 (3.8) Moderate: 15 (7.2) Severe: 9 (4.3)
				RT + surg 50.4 Gy (44 to 66): 88 (42.0)	163			> 30 years old, 5-yr:75.0			
Keus et al 2013[22]	44	2001 to 2008	Inoperable progressive disease of primary, recurrent or incompletely resected lesions	RT (56Gy): 44 (100.0)	57.6	NE	CR: 6 (13.6) PR: 16 (36.4) SD: 18 (40.9) PD: 3 (6.8) Not assessable: 1 (2.3)	3-yrs: 81.5	NE	NE	Skin toxicity 18 (41.0) Lymphedema 10 (23.0) Pain 8 (18.0)

Isolated limb perfusion										
Author, year	**Patients: procedures, n**	**Period**	**Inclusion criteria**	**Type of treatment (dose), n (%)**	**Median follow-up, mths**	**Local control, n (%)**	**RECIST response, n (%)**	**ORR, %**	**Functional outcome, n (%)**	**Toxicity, n (%)**
Grunhagen et al 2005[23]	11:12	1991 to 2003	Locally advanced	ILP (TNF 4-3 mg + melphalan	31	10/12 (83.0)	CR: 2 (17.0) PR: 7 (58.0)	75.0	No physical limitations: 7 (64)	Local toxicity: 4 (36.0)

			desmoid tumours	10 to 13 mg/l limb): 11 (100.0)					Mildly disturbed: 3(27) No further functional loss: 1 (9) Amputation: 0	(grade III) Systemic toxicity: 0
van Broekhoven et al 2014[24]	25:28	1990 to 2012	Consecutive patients with aggressive fibromatosis	ILP: 25 (100.0)	84	4/25 (16.0)	CR: 2 (8.0) PR: 16 (64.0) SD: 7 (28.0)	72.0	No physical limitations: 16 (64.0) Some limitations but not need medical aids: 6 (24.0) Amputation: 3 (12.0)	Local toxicity 8/28 (29.0) (6, grade III; 2, grade IV)
Cryoablation										
Author, year	**Patients: procedures, n**	**Period**	**Inclusion criteria**	**Type of treatment (dose), n (%)**	**Median FU, mths**	**PFS, %**	**RECIST response, n (%)**	**ORR, %**	**Functional outcome, n (%)**	**Toxicity n (%)**
Auloge et al 2021[25]	30:34	2007 to 2019	Consecutive patients with symptomatic desmoid tumours evolving after "wait and watch" periods, and despite	CA: 30 (100.0)	18.5	1-yr: 85.1 3-yr: 77.3	CR: 13 (43.3) PR: 11 (36.7) SD: 1 (3.0) PD: 5 (17.0)	80.0	Significant reduction of pain: 29 (96.7%) All patient with a functional disability (53.0%) demonstrated	Adverse events: 11 (36.6) Major complication: 4 (13.3)

			medical treatment						symptomatic improvement	
Efrima et al 2021[26]	11:16	2016 to 2019	Desmoid tumours that showed progression of size; symptomatic tumours"	CA: 11 (100.0)	NE	NE	NE	NE	Symptomatic improvement : 9/11 (82.0%)	Mild complications : 3/16 (19.0)
Kurtz et al 2021[27]	50	2015 to 2017	Non-abdominopelvic progressing DT; Progressive disease after > two lines of medical therapy or with functional symptoms/pain	CA: 50 (100.0)	31	1-yr: 85.8	CR: 12/42 (28.6) PR: 11/42 (26.2) SD: 13/42 (31.0)	54.8	Cryoablation significantly improved functional status and pain scores	G1: 31 (62.0) G2: 29 (58.0) G3: 11(22.0) G4: 4 (8.0) G5: 0

CR, complete response; CA, cryoablation; FU, follow-up; ILP, isolated limb perfusion; LR, local recurrence; NE, not evaluated; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumor; RT, radiotherapy; SD, stable disease; surg, surgery; TNF, tumor necrosis factor.

Table iv. An overview of the available evidence regarding different treatments for desmoid tumours: surgery.

Author, year	Patients, n	Period	Inclusion criteria	Type of treatment, n (%)	Median follow-up, mths	OS, %	Surgical margins, n (%)*	LR, n (%)	LRFS, %	DFS, %
Gronchi et al 2003[28]	203	1966 to 2001	Consecutive patients treated with surgery	Surg: 203 (100.0)	135	5-yr: 98.0 10-yr: 94.0	R0: 146 (72.0) R1: 57 (28.0) R2: 0	55/203 (27.0	NE	5-yr: 73.0 10-yr: 70.0

Salas et al 2011[29]	426	1965 to 2008	Consecutive patients with sporadic aggressive fibromatosis	Surg ±RT: 370 (86.9) RT: 6 (1.4)	NE	NE	R0: 111 (30) R1: 110 (29.7) R2: 37 (8.6)	143/323 (44.3%)	NE	NE
Crago et al 2013[30]	495	1982 to 2011	Primary or locally recurrent desmoids	Surg: 495 (100.0)	60	NE	R0/R1: 439 (88.7) R2: 53 (11.0)	110/439 (23.0)	5-yr: 69.0	NE

*Surgical margins: R2, macroscopic incomplete resection; R1, microscopic incomplete resection; R0, microscopic complete resection.

DFS, disease-free survival; FU, follow-up; LR, local recurrence; LRFS, local recurrence-free survival; NE, not evaluated; OS, overall survival; RT, radiotherapy; surg, surgery.

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