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Sarcomas

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Institut Jules Bordet
Brussels, Belgium

12th Belgian Symposium on the Integration of Molecular Biology Advances into Oncology Clinical Practice and Post-MASCC
23e Novembre 2018

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Disclosures

- Travel expenses : Pharmamar, Bayer, Pfizer

Summary

- Introduction
- What's new in 2018 in sarcoma management
- Future perspectives / promising molecules

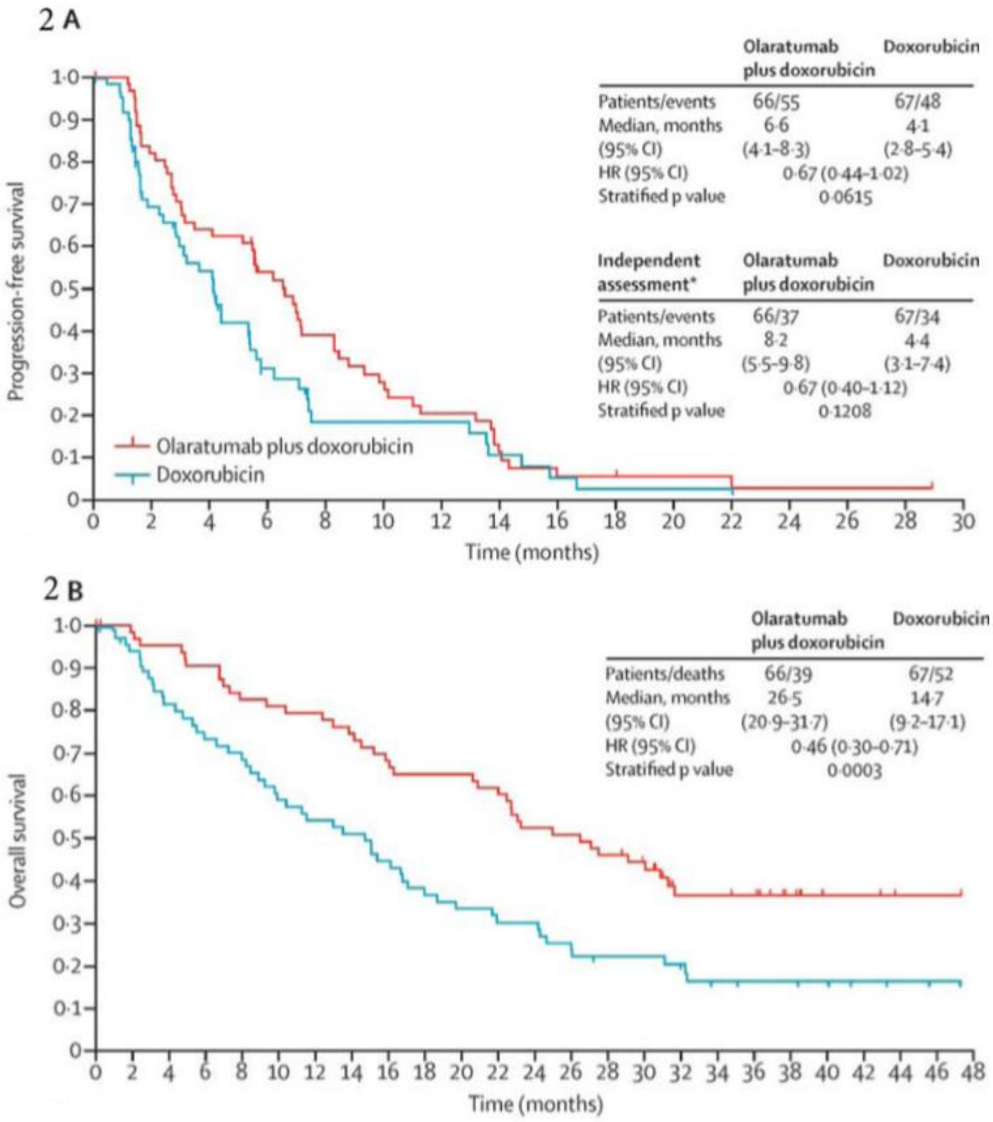
Sarcoma

- Rare solid tumors ; incidence 2-5/100.000/year
- Sub-groups
  - Soft tissue sarcoma
  - Bone sarcoma
  - GIST
- Diverse group of tumors originating from mesenchymal precursors
- ~ 1% of all adult malignancies

What’s new in 2018 in sarcoma management

Olaratumab : reimbursement

- Phase 1b/2
- Recombinant human IgG1 monoclonal antibody that specifically binds PDGFRα
- Results of phase 3 trial avaiting !
- 34% of tumors were positive for PDGFRα
- The interaction effect between PDGFRα expression (positive or negative) and treatment was not significant for either overall or progression-free survival



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Tap WD et al., Lancet. 2016 Jul 30;388(10043):488-97

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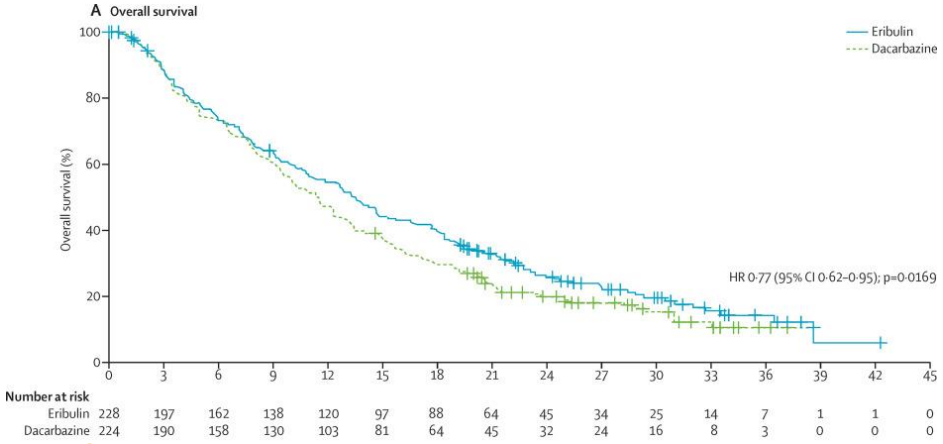
Eribulin : reimbursement

Eribulin versus dacarbazine in previously treated patients with advanced liposarcoma or leiomyosarcoma: a randomised, open-label, multicentre, phase 3 trial

- Intermediate-grade or high-grade advanced liposarcoma or leiomyosarcoma
- At least two previous systemic regimens for advanced disease (including an anthracycline)



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Schöffski et al., Lancet 2016 Apr 16;387(10028):1629-37

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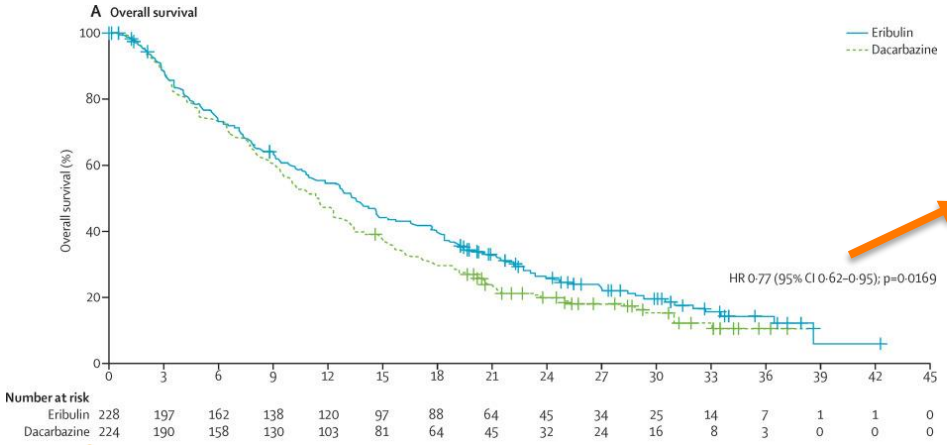
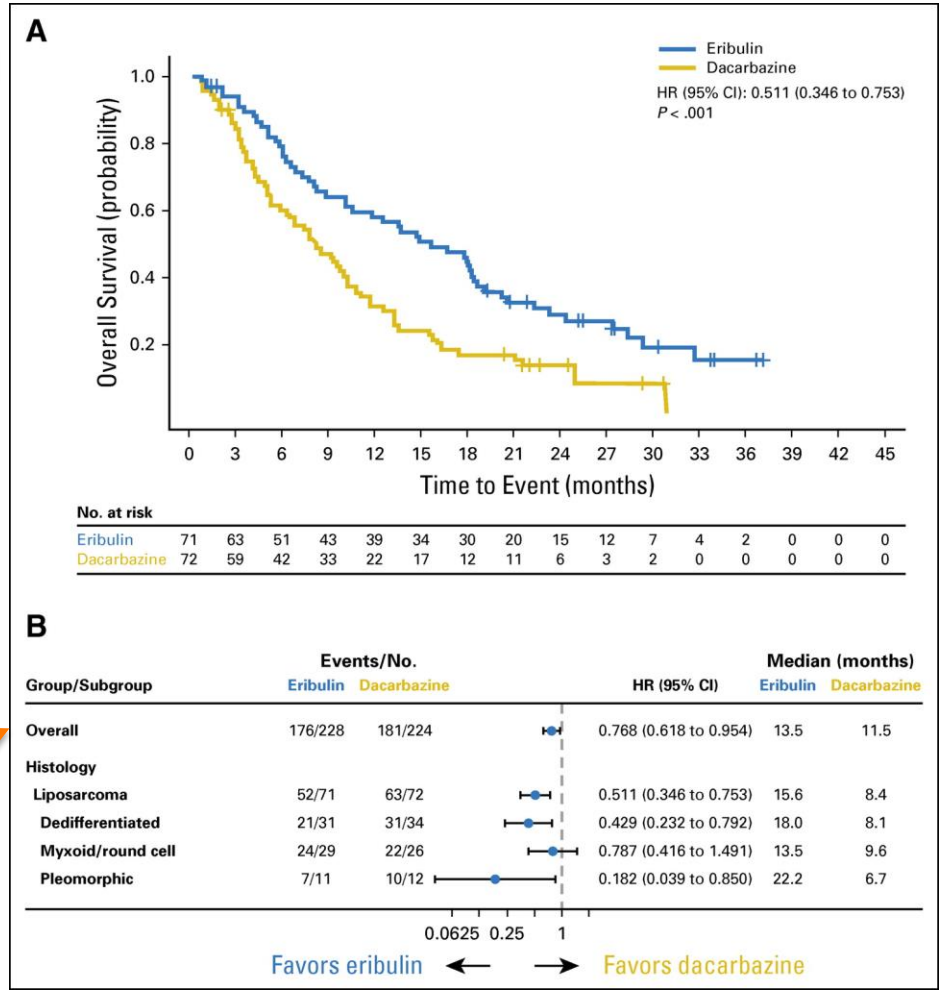
Eribulin : reimbursement

Eribulin versus dacarbazine in previously treated patients with advanced liposarcoma or leiomyosarcoma: a randomised, open-label, multicentre, phase 3 trial

Activity of Eribulin in Patients With Advanced Liposarcoma Demonstrated in a Subgroup Analysis From a Randomized Phase III Study of Eribulin Versus Dacarbazine

- Intermediate-grade or high-grade advanced liposarcoma or leiomyosarcoma
- At least two previous systemic regimens for advanced disease (including an anthracycline) ≠ !





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Schöffski et al., Lancet 2016 Apr 16;387(10028):1629-37
Demetri GD et al., J Clin Oncol. 2017 Oct 20;35(30):3433-3439

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New ESMO Guidelines

Annals of Oncology 29 (Supplement 4): iv51–iv67, 2018
doi:10.1093/annonc/mdy096
Published online 28 May 2018

CLINICAL PRACTICE GUIDELINES

Soft tissue and visceral sarcomas: ESMO–EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up†

P. G. Casali[1], N. Abecassis[2], S. Bauer[3], R. Biagini[4], S. Bielack[5], S. Bonvalot[6], I. Boukovinas[7], J. V. M. G. Bovee[8], T. Brodowicz[9], J. M. Broto[10], A. Buonadonna[11], E. De Álava[10], A. P. Dei Tos[12], X. G. Del Muro[13], P. Dileo[14], M. Eriksson[15], A. Fedenko[16], V. Ferraresi[17], A. Ferrari[18], S. Ferrari[19], A. M. Frezza[1], S. Gasperoni[20], H. Gelderblom[21], T. Gil[22], G. Grignani[23], A. Gronchi[1], R. L. Haas[24], A. Hannu[25], B. Hassan[26], P. Hohenberger[27], R. Issels[28], H. Joensuu[29], R. L. Jones[30], I. Judson[31], P. Jutte[32], S. Kaal[33], B. Kasper[27], K. Kopeckova[34], D. A. Krákorová[35], A. Le Cesne[36], I. Lugowska[37], O. Merimsky[38], M. Montemurro[39], M. A. Pantaleo[40], R. Piana[41], P. Picci[19], S. Piperno-Neumann[6], A. L. Pousa[42], P. Reichardt[43], M. H. Robinson[44], P. Rutkowski[37], A. A. Safwat[45], P. Schöffski[46], S. Sleijfer[47], S. Stacchiotti[48], K. Sundby Hall[49], M. Unk[50], F. Van Coevorden[51], W. Van der Graaf[30], J. Whelan[52], E. Wardelmann[53], O. Zaikova[54] & J. Y. Blay[55], on behalf of the ESMO Guidelines Committee and EURACAN*

Annals of Oncology 29 (Supplement 4): iv68–iv78, 2018
doi:10.1093/annonc/mdy095
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CLINICAL PRACTICE GUIDELINES

Gastrointestinal stromal tumours: ESMO–EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up†

P. G. Casali[1], N. Abecassis[2], S. Bauer[3], R. Biagini[4], S. Bielack[5], S. Bonvalot[6], I. Boukovinas[7], J. V. M. G. Bovee[8], T. Brodowicz[9], J. M. Broto[10], A. Buonadonna[11], E. De Álava[10], A. P. Dei Tos[12], X. G. Del Muro[13], P. Dileo[14], M. Eriksson[15], A. Fedenko[16], V. Ferraresi[17], A. Ferrari[18], S. Ferrari[19], A. M. Frezza[1], S. Gasperoni[20], H. Gelderblom[21], T. Gil[22], G. Grignani[23], A. Gronchi[1], R. L. Haas[24], A. Hannu[25], B. Hassan[26], P. Hohenberger[27], R. Issels[28], H. Joensuu[29], R. L. Jones[30], I. Judson[31], P. Jutte[32], S. Kaal[33], B. Kasper[27], K. Kopeckova[34], D. A. Krákorová[35], A. Le Cesne[36], I. Lugowska[37], O. Merimsky[38], M. Montemurro[39], M. A. Pantaleo[40], R. Piana[41], P. Picci[19], S. Piperno-Neumann[6], A. L. Pousa[42], P. Reichardt[43], M. H. Robinson[44], P. Rutkowski[37], A. A. Safwat[45], P. Schöffski[46], S. Sleijfer[47], S. Stacchiotti[48], K. Sundby Hall[49], M. Unk[50], F. Van Coevorden[51], W. Van der Graaf[30], J. Whelan[52], E. Wardelmann[53], O. Zaikova[54] & J. Y. Blay[55], on behalf of the ESMO Guidelines Committee and EURACAN*

Bone sarcomas: ESMO–PaedCan–EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up†

P. G. Casali‡1, S. Bielack‡2, N. Abecassis[3], H.T. Aro[4], S. Bauer[5], R. Biagini[6], S. Bonvalot[7], I. Boukovinas[8], J. V. M. G. Bovee[9], B. Brennan[10], T. Brodowicz[11], J. M. Broto[12], L. Brugières[13], A. Buonadonna[14], E. De Álava[15], A. P. Dei Tos[16], X. G. Del Muro[17], P. Dileo[18], C. Dhooge[19], M. Eriksson[20], F. Fagioli[21], A. Fedenko[22], V. Ferraresi[6], A. Ferrari[23], S. Ferrari[24], A. M. Frezza[25], N. Gaspar[13], S. Gasperoni[26], H. Gelderblom[27], T. Gil[28], G. Grignani[29], A. Gronchi[1], R. L. Haas[30], B. Hassan[31], S. Hecker-Nolting[2], P. Hohenberger[32], R. Issels[33], H. Joensuu[34], R. L. Jones[35], I. Judson[36], P. Jutte[37], S. Kaal[38], L. Kager[39], B. Kasper[32], K. Kopeckova[40], D. A. Krákorová[41], R. Ladenstein[39], A. Le Cesne[13], I. Lugowska[42], O. Merimsky[43], M. Montemurro[44], B. Morland[45], M. A. Pantaleo[46], R. Piana[21], P. Picci[24], S. Piperno-Neumann[7], A. L. Pousa[47], P. Reichardt[48], M. H. Robinson[49], P. Rutkowski[42], A. A. Safwat[50], P. Schöffski[51], S. Sleijfer[52], S. Stacchiotti[25], S. J. Strauss[18], K. Sundby Hall[53], M. Unk[54], F. Van Coevorden[55], W.T.A. van der Graaf[35,38,55], J. Whelan[18], E. Wardelmann[56], O. Zaikova[57] & J. Y. Blay[58], on behalf of the ESMO Guidelines Committee, PaedCan and ERN EURACAN*

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Casali PG et al., *Annals of Oncology*, Volume 29, Issue Supplement_4, 1 October 2018, Pages iv51–iv67
Casali PG et al., *Annals of Oncology*, Volume 29, Issue Supplement_4, 1 October 2018, Pages iv68–iv78
Casali PG et al., *Annals of Oncology*, Volume 29, Issue Supplement_4, 1 October 2018, Pages iv79–iv95

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Future perspectives

Promising molecules

Immunotherapy and sarcomas

- Characteristics that may facilitate response to immunotherapy :
  - Inflammatory signature, PDL, TILS, mutational load?
- Few neo-antigens → few responses to CPI
- Expression of immunogenic proteins and antigens
  - Cancer-testis antigen family
    (NY-ESO-1, MAGE-A3, PRAME, LAGE-1)
  - Gangliosides
    (GM2, GD2, GD3)
  - Sarcoma Specific Fusion Proteins
    (SSX, FOXO1, EWSR1, TLS CHOP)
  - Heat shock proteins
- Limitations : rare and heterogeneous tumors

Table 2 Reported PD-L1 expression in some sarcoma

Sarcoma subtype	Positive cases (%)
Angiosarcoma	50–80
Chondrosarcoma	41–75
Ewing sarcoma	29–67
Leiomyosarcoma	32–70
Malignant peripheral nerve sheath tumor	17–67
Osteosarcoma	28–57
Rhabdomyosarcoma	38–63
Synovial sarcoma	25–75
Dedifferentiated liposarcoma	67–82
Gastrointestinal stromal tumor	29

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Mitsis D et al. Sarcoma. 2016;2016:9757219. Epub 2016 Sep 14
Veenstra R et al. Lab Invest. 2018 Jan;98(1):41-50

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Durvalumab plus tremelimumab shows modest activity for advanced sarcoma

- 46 patients
- 5 PR :
  - 1 UPS (25%)
  - 1 angiosarcoma (20%)
  - 3 alveolar soft par sarcoma (50%)
- Disease control rate alveolar soft part sarcoma : 83%
- OS 14.5 mois, PFS 4.1 mois

New ASPS Clinical Trial: Axitinib and Pembrolizumab in Subjects With Advanced Alveolar Soft Part Sarcoma and Other Soft Tissue Sarcomas

	Best overall response, N (%)
All patients (N=29)	PR 5 (17) SD 9 (31) PD 15 (52)
ASPS (N=9)	PR 4 (44) SD 3 (33) PD 2 (22)
Non-ASPS (N=20)	PR 1 (5) SD 6 (30) PD 13 (65)

Nivolumab with or without ipilimumab treatment for metastatic sarcoma (Alliance A091401): two open-label, non-comparative, randomised, phase 2 trials

Confirmed responses :

2 (5%) des 38 patients du groupe nivolumab

6 (16%) des 38 patients du groupe nivolumab plus ipilimumab

PHASE II STUDY OF ATEZOLIZUMAB IN PATIENTS WITH ALVEOLAR SOFT PART SARCOMA

18 pts : PRs was observed in 7/18 pts (39%) with 5/7 pts (28%) having a confirmed PR

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Somaiah N., presentation at CTOS 2017
Wilky BA, presentation at CTOS 2017
D'Angelo SP et al. Lancet Oncol. 2018 Mar;19(3):416-426
O'Sullivan Coyne G, presentation at CTOS 2018

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Immune response, safety, and survival impact from CMB305 in NY-ESO-1+ recurrent soft tissue sarcomas (C131 study)

- **LV305 Priming:**
  - **Dendritic cell (DC) targeting NY-ESO-1 lentiviral vector encoding full length NY-ESO-1**
  - Integration deficient, replication incompetent
  - Induces and expands NY-ESO-1 specific CD8 and CD4 T Cells
- **G305 boosting:**
  - **Potent TLR-4 agonist** co-formulated with **NY-ESO-1 full length protein**
  - Enhances LV305 immunogenicity and triggers anti-NY-ESO-1 antibodies

CMB305 is an active immunotherapy regimen designed to generate and expand anti-NY-ESO-1 T and B cells

	STS (N=25)	Synovial sarcoma (N=15)	Myxoid/round cell sacroma (N=8)
Overall response rate, N (%)	0	0	
Stable disease, N (%)	17 (68)	8 (57)	6 (75)
PFS, median months	3.9	3.7	
6-months PFS rate, %	33.3	30.8	
12-months PFS rate, %	20.8	23.1	
Median OS, months		23.7	29.2

→ Randomized phase II with atezolizumab (IMDZ-C232) = closed
→ Randomized phase III as maintenance after chemotherapy (IMDZ-04-1702) = stopped

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Chawla SP et al., Annals of Oncology (2018) 29 (suppl_8): viii576-viii595. 10.1093/annonc/mdy299

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Immunotherapy and sarcomas

- CPI monotherapy : deception
- Combinations and adoptive cellular therapy :
  - more promising
  - promising for certain types of sarcomas

A phase 2, multicenter study of the EZH2 inhibitor tazemetostat in adults (INI1-negative tumors cohort) (NCT02601950)

Endpoint Category, n (%)	Total N=32
ORR (CR + PR)	3 (9)
95% CI	2.0–25.0
Best response	
CR	0
PR	3 (9)
SD	13 (41)
PD	10 (31)
Non-evaluable, missing, or unknown	6 (19)

→ Sarcomas : 13

→ 2 of 2 spindle cell sarcomas

- Integrase interactor 1 (INI1) = SWI/ SNF subunit
- SWI/SNF = ATP-dependant chromatin remodeling complexe, restructuring the nucleosome to make its DNA accessible during transcription, replication and DNA repair
- INI1 loss can induce tumor dependence on enhancer of zeste homolog 2 (EZH2), a histone methyltransferase
- Tazemetostat = potent, selective, oral EZH2 inhibitor

A phase 2, multicenter study of the EZH2 inhibitor tazemetostat in adults: (epithelioid sarcoma cohort) (NCT02601950)

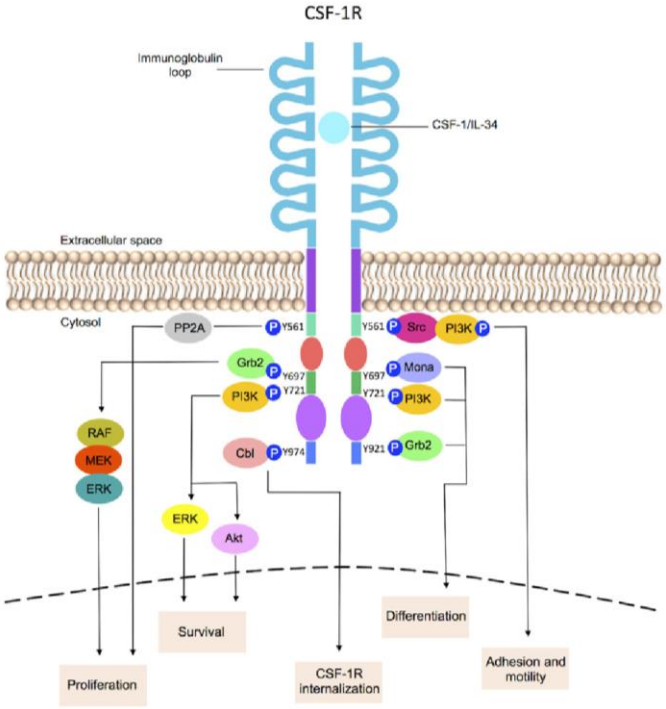
Endpoint Category, n (%)	No Prior Anticancer Therapy N=24	Prior Anticancer Therapy N=38	Total N=62
DCR [CR + PR + (SD≥32 weeks)]	9 (38)	6 (16)	15 (24)
ORR (CR + PR)	5 (21)	3 (8)	8 (13)
Best Response			
CR	0	0	0
PR	5 (21)	3 (8)	8 (13)
SD	16 (67)	20 (53)	36 (58)
PD	2 (8)	11 (29)	13 (21)
NE, missing, or unknown	1 (4)	4 (11)	5 (8)

Stacchiotti S et al., Annals of Oncology (2018) 29 (suppl_8): viii576-viii595. 10.1093/annonc/mdy299
Gounder M et al., Annals of Oncology (2018) 29 (suppl_8): viii576-viii595. 10.1093/annonc/mdy299

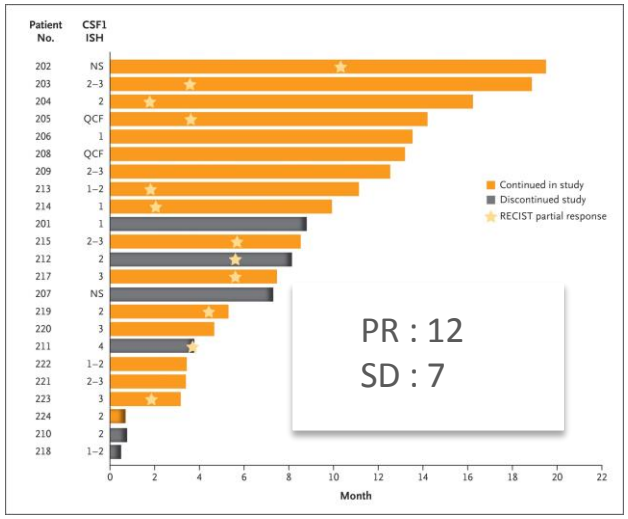
Structure-Guided Blockade of CSF1R Kinase in Tenosynovial Giant-Cell Tumor

= pigmented villonodular synovitis/PVNS

- Characterized by a proliferation of synoviocytes
- Marked by a disease specific fusion involving the colony-stimulating factor 1 receptor gene (CSF1R)



- PLX3397 = Pexidartinib
  - potent, selective CSF1R inhibitor
- Phase I/II trial
  - 41 pts in dose-escalation part → 1000mg/day
  - 23 pts in extension part



- Phase III trial (ENLIVEN study) vs placebo
  - 120 pts → ORR : 55.7%

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Tap WD et al., N Engl J Med. 2015 Jul 30;373(5):428-37
Tap WD, phase III data presented at ASCO 2018

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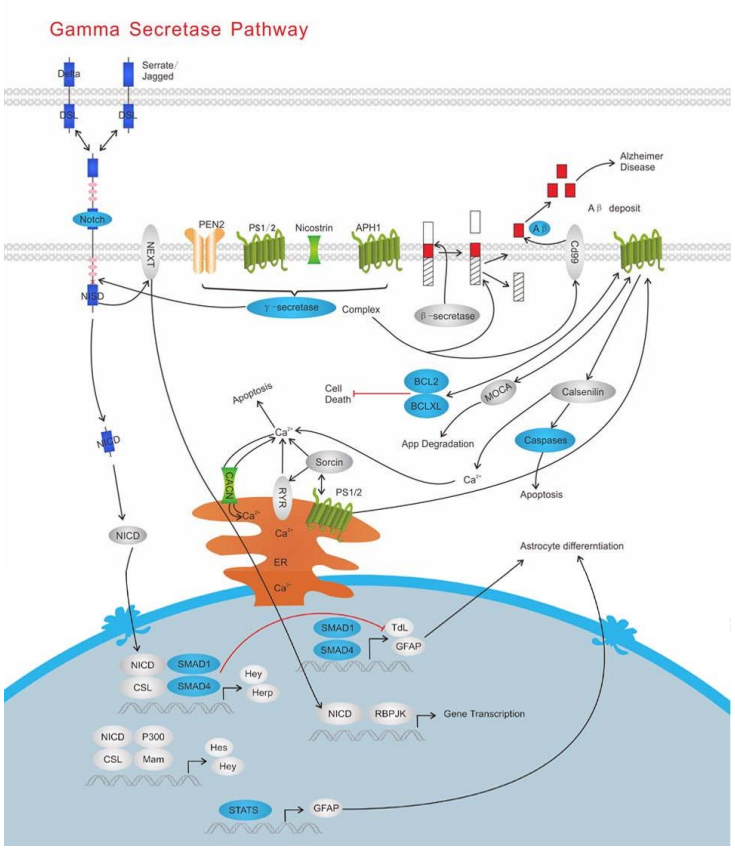
November 08, 2018

Nirogacestat Gets Fast-Tracked for the Treatment of Desmoid Tumors

- Potent, selective, reversible, noncompetitive inhibitor of gamma-secretase (GS)
- Phase I: solid tumors + hematologic
  - Best tumor responses were 5 PRs of 7 evaluable patients with desmoid tumors
  - The 5 patients maintained response 48-73 months
- Phase II: desmoid tumors/aggressive fibromatosis
  - 17 patients received daily doses of nirogacestat at 150 mg BID continuously for 3 week cycles
  - 16 patients were evaluable for response
  - 5 patients experienced confirmed PR
  - 11 patients had stable disease
- Phase III : Nirogacestat vs placebo in progressing desmoid tumors/aggressive fibromatosis
  - Planned



Kummar S et al., J Clin Oncol. 2017 May 10;35(14):1561-1569

ACTIVITY OF LAROTRECTINIB IN SARCOMA PATIENTS WITH TRK FUSION CANCER

- Tropomyosin receptor kinases (TRKs) are encoded by neurotrophic tyrosine receptor kinase genes (NTRKs)
- Aberrant genomic translocations involving NTRK genes have been shown to give rise to constitutively active, oncogenic TRK fusion proteins
- Larotrectinib is a potent and highly selective TRK inhibitor

- As of February 19 2018 : 32 pts with TRK fusion sarcoma
  - 17 soft tissue sarcomas (STS)
  - 10 infantile fibrosarcoma (IFS)
  - 5 gastrointestinal stromal tumors (GIST)
- ORR 91% overall
  - 88% in STS (15/17)
  - 90% in IFS (9/10)
  - 100% in pts with GIST (5/5)
  - **6 CR**

- 8 distinct NTRK gene fusions were detected, ETV6-NTRK3 fusion being the most common (11 pts)
- Other fusions identified included : TPM3-NTRK1,LMNA-NTRK1, LMNA-NTRK3, PDE4DIP-NTRK1, SQSTM1NTRK1, STRN-NTRK2, and TPM4-NTRK3

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Federman N., presentation at CTOS 2018

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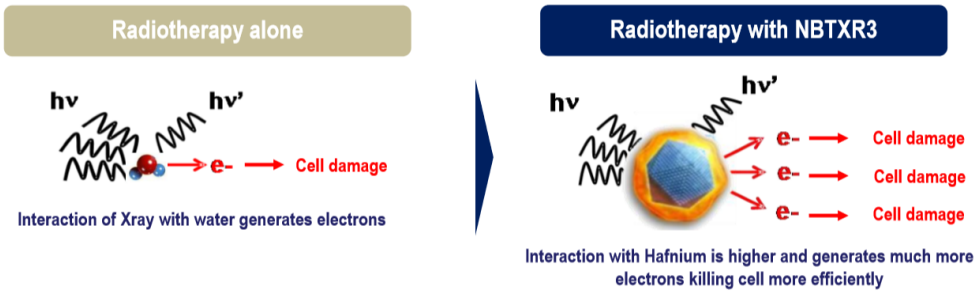
A PHASE II/III TRIAL OF HAFNIUM OXIDE NANOPARTICLES ACTIVATED BY RADIOTHERAPY IN THE TREATMENT OF LOCALLY ADVANCE SOFT TISSUE SARCOMA OF THE EXTREMITY AND TRUNK WALL

MUNICH 2018 ESMO congress



NBTXR3 is a first in class radio-enhancer with a physical mode of action increasing the dose absorbed by 9x around clusters, triggering more cell damage*

- Primary endpoint : pCRR
  Main secondary endpoint : quality of surgery-R0 rate } achieved
- Grade 3-4 acute immune reactions in 7.9% of patients, manageable and of short duration
- RT safety profile similar in both arms, including postsurgical wound complications

Phase II/III randomized, multi-center, open-label and active controlled two arms study

Soft Tissue sarcoma (STS) of the extremity and trunk wall

- Age ≥ 18 years-old
- Locally advanced soft tissue sarcoma, newly diagnosed or relapsed tumor
- High-risk tumor
- Unresectable tumor or unfeasible carcinological surgical resection
- WHO score of 0 to 2

R 1:1

- Arm A: NBTXR3* activated by EBRT**
- Arm B: EBRT** alone

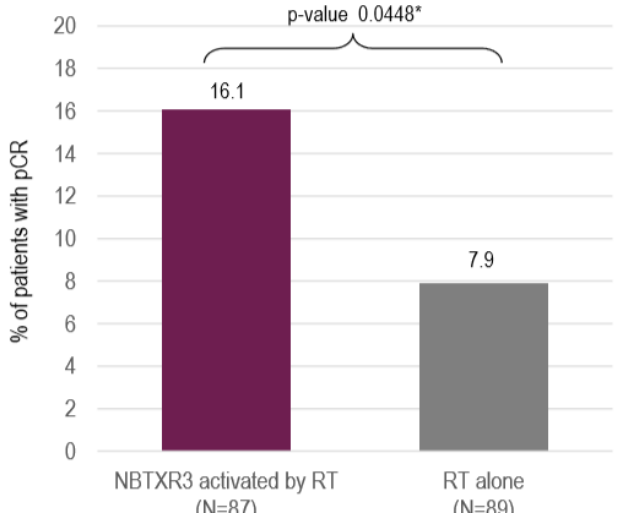
N=180 randomized §

32 sites in 11 countries in Europe and Asia

Primary endpoint:
- Pathological complete response rate# (pCRR) following EORTC Guidelines(1)

Secondary endpoints:
- Safety
- Carcinologic resection (surgical margin, R0, …)
- Pathological Response (pR)
- Amputation rate

Stratification:
- Myxoid liposarcoma / other



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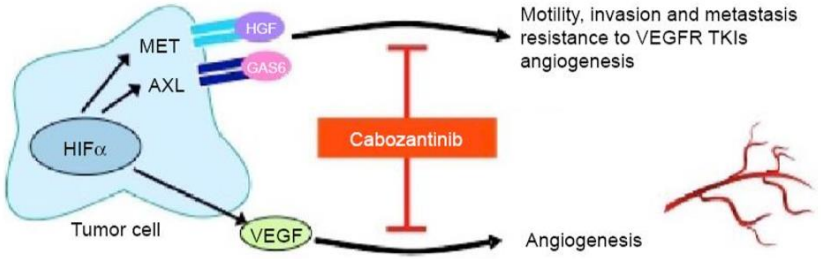
Bonvalot S, Proffered paper session, ESMO 2018

CABOZANTINIB IN PATIENTS WITH ADVANCED OSTEOSARCOMAS AND EWING SARCOMAS

MUNICH 2018 ESMO congress

A French Sarcoma Group (FSG)/ US National Cancer Institute phase II collaborative study.

- Cabozantinib : potent, orally bioavailable, multitargeted, small-molecule inhibitor of VEGFR-2, AXL, c-MET
- Aberrant angiogenesis
  - common feature of Ewing and osteosarcomas
- MET overexpression
  - frequent
  - associated with adverse outcome



Approved for
- RCC
- MTC

Cabozantinib has demonstrated the highest antitumor activity ever observed in single-arm studies including osteosarcoma and Ewing's sarcoma patients with heavily pre-treated advanced disease

	Osteosarcomas (n=41)	Ewing's sarcomas (n=32)
Tumor burden reduction ate	41%	71%
Objective response rate	11.9%	28.1%
Median PFS (months)	6.2	5.2
Median OS (months)	10.6	9.8

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Italiano A, Proffered paper session, ESMO 2018

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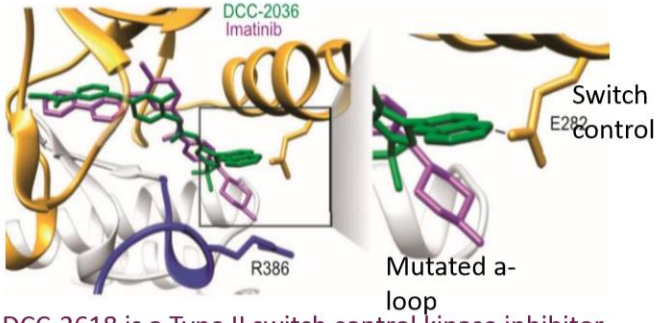
Initial Results of Phase 1 Study of DCC-2618, a Broad-spectrum KIT and PDGFRα Inhibitor, in Patients (pts) with Gastrointestinal Stromal Tumor (GIST) by Number of Prior Regimens.

- Secondary resistance to first-line imatinib
  - eventually develops over the course of treatment in about 80% of responding patients
  - mostly due to KIT exon 13, 17 and 18 mutations



DCC-2618 is a Type II switch control kinase inhibitor - Acts in a ATP-noncompetitive manner.

DCC-2618 Results Provided Encouraging Efficacy across all Lines of Treatment ≥100 mg/d (n=178)

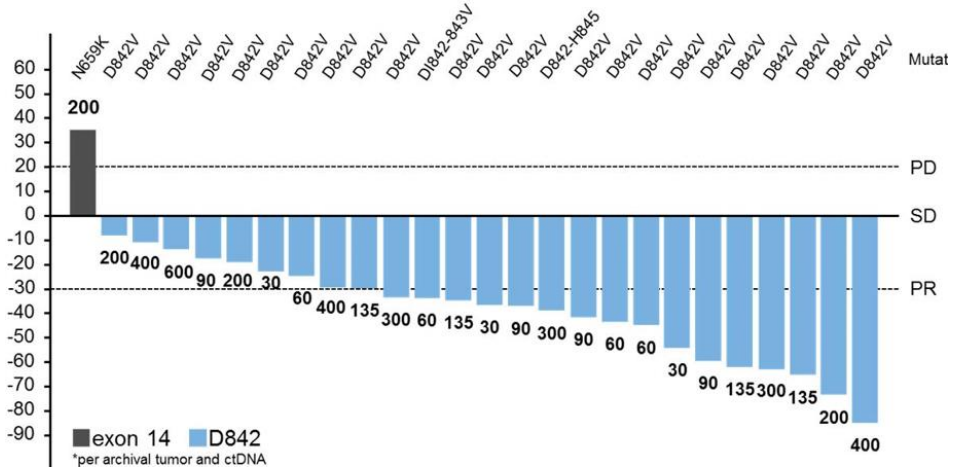
Line of Therapy	Objective Response Rate[1]	Disease Control Rate @ 3 Months	Median Progression Free Survival (mPFS)	Censored Patients for mPFS	Median Treatment Duration[4]
2nd Line (n=38)	18%[2] (7/38)	79%	42 weeks (24, NE)	58%	48 weeks (31, NE)
3rd Line (n=29)	24% (7/29)	83%	40 weeks (24, NE)	52%	NR (36, NE)
≥4th Line (n=111)	9% (10/106)[3]	66%	24 weeks (16, 30)	35%	28 weeks (22, 47)
2nd & 3rd Line (n=67)	21%(2) (14/67)	81%	40 weeks (24, NE)	55%	52 weeks (36, NE)

George S, Proffered paper session, ESMO 2018

Clinical activity of BLU-285 in advanced gastrointestinal stromal tumor (GIST)

ASCO ANNUAL MEETING '17

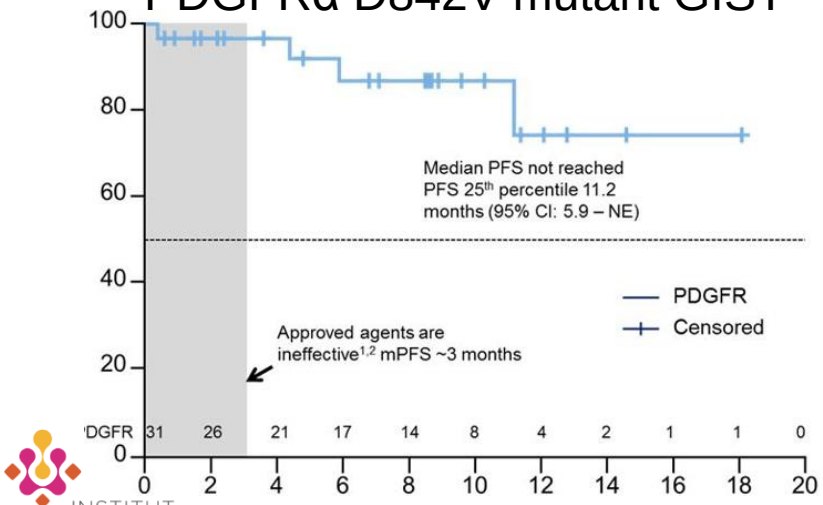
PDGFRα D842V-mutant GIST



PDGFRα D842V-mutant GIST

Best response (N=25)	Choi Criteria n (%)	RECIST 1.1 n (%)
PR	25 (100%)	15* (60%)
SD	0	10 (40%)
DCR (PR + SD)	25 (100%)	25 (100%)
PD	0	0

PDGFRα D842V-mutant GIST



Heavily pre-treated KIT-mutant GIST

Best response (N=25)	Choi Criteria n (%)	RECIST 1.1 n (%)
PR	8 (32)	2* (8)
SD	6 (24)	12 (48)
DCR (PR + SD)	14 (56)	14 (56)
PD	11 (44)	11 (44)

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Heinrich M., Abstract no: 11011, presentation at ASCO 2017

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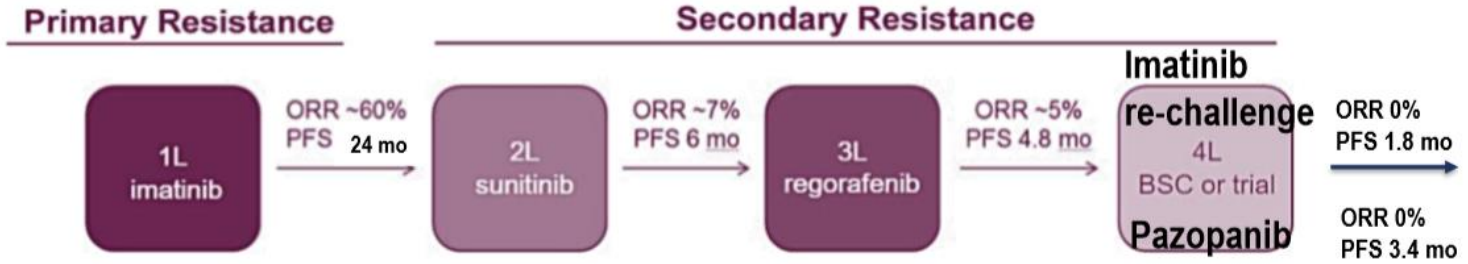
New agents in clinical trials beat the treatment paradigm in GIST



Reimbursed

Phase 1 data

DCC-2618 ORR 18% mPFS 10.5 mo

DCC-2618 ORR 24% mPFS 10 mo

DCC-2618 ORR 9% mPFS 6 mo

Avapritinib (BLU-285) ORR 8% (Choi 32%) mPFS 9.3 mo

Phase III trials

Study name	Study drug	Planned size; Randomization	Eligibility	Study number
INVICTUS	DCC2618 vs Placebo	120; 2:1	≥4th line GIST	NCT03353753
INTRIGUE	DCC2618 vs Sunitinib	358;1:1	2nd line GIST	NCT03673501
VOYAGER	AVAPRITINIB vs Regorafenib	460; 1:1	3nd and 4th line GIST	NCT03465722
CRENOGIST	CRENOLANIB vs Placebo	120; 2:1	D842V Mutated PDGFRA Gene	NCT02847429

Katz D, Proffered paper session, ESMO 2018

Conclusions I

- New reimbursements
  - Olaratumab : STS, in combination with Doxorubicin (1st line)
  - Eribulin : liposarcoma, ≥ 2d line

Conclusions II

- Promising molecules
  - CPI in combination?
  - CMB305 : NY-ESO-1+ STS / SS
  - Tazemetostat : INI1- tumors, epithelioid sarcoma
  - Pexidartinib : PVNS
  - Nirogacestat : desmoid
  - Larotrectinib : sarcoma with TRK fusion
  - Nanoparticles in combination with RT : locally advanced STS
  - Cabozantinib : bone sarcomas
  - DCC-2618 : GIST
  - BLU-285 : GIST

Conclusions II

- Promising molecules
  - CPI in combination?
  - CMB305 : NY-ESO-1+ STS / SS
  - Tazemetostat : INI1- tumors, epithelioid sarcoma
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  - Nanoparticles in combination with RT : loca ced STS
  - Cabozantinib : bone sarcomas
  - DCC-2618 : GIST
  - BLU-285 : GIST

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Thank you for your attention

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