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# ESMO SARCOMA AND RARE CANCERS

Annual Congress

## IMPACT OF NIROGACESTAT ON PATIENT-REPORTED OUTCOMES IN ADULTS WITH DESMOID TUMOR WITH A BEST OVERALL RESPONSE OF STABLE DISEASE: POST HOC ANALYSIS FROM THE DeFi STUDY

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# DECLARATION OF INTERESTS

Silvia Stacchiotti reports\*:

Personal financial interests (honoraria, consultancy, or advisory role) from: Aadi, Astex Pharmaceuticals, Bavarian Nordic, Bayer, Boehringer Ingelheim, Daiichi Sankyo, Deciphera, Epizyme, Gentili, Glaxo, Ikena, Ipsen, Maxivax, Novartis, PharmaMar, RainThera, and Servier

Institutional and financial interests from: Advenchen, Bayer, Boehringer Ingelheim, Blueprint, Daiichi Sankyo, Deciphera, Epizyme, Eli Lilly, Glaxo, Hutchinson, Karyopharm, Novartis, PharmaMar, RainTher, and SpringWorks.

*\*last 3 years*

# DESMOID TUMORS

- ◆ **Rare, locally invasive, soft-tissue tumors with unpredictable disease course<sup>1</sup>**
  - Can result in severe pain, functional impairment, decreased QoL, and other complications
  
- ◆ **Treatment goals should extend beyond radiologic response and assess quality of life improvements, including PROs such as<sup>1,2</sup>:**
  - Pain and DT symptom burden
  - Functioning with daily activities
  - Overall QoL

DT, desmoid tumor; PROs, patient-reported outcomes; QoL, quality of life.

<sup>1</sup>Bektas M, et al. *Adv Ther.* 2023;40(9):3697-3722. <sup>2</sup>Gounder MM et al. *Cancer.* 2020;126(3):531-539.

# NIROGACESTAT AND THE PHASE 3 DeFi STUDY

- ◆ **Nirogacestat**, selective gamma secretase inhibitor<sup>1</sup>
  - First treatment approved in the United States for adults with progressing DT<sup>2</sup>

**Objective: Assess improvement in PROs with niro vs pbo in pts with stable disease as best overall response, using post hoc analyses**

**Progression-free survival** (HR: 0.29, 95% CI: 0.15–0.55,  $P < .001$ )

**Objective response rate** (41% niro vs 8% pbo;  $P < .001$ )

**PROs:** pain, DT-specific symptom burden, physical & role functioning, and overall QoL ( $P \leq .01$  all at cycle 10)

BID, twice daily; CI, confidence interval; DT, desmoid tumor; HR, hazard ratio; niro, nirogacestat; pbo, placebo; PRO, patient-reported outcome; pts, patients; QoL, quality of life; RECIST, Response Evaluation Criteria in Solid Tumors. <sup>a</sup>Datacut: 07Apr2022.

<sup>1</sup>Gounder MM, et al. *N Engl J Med*. 2023;388(10):898-912. <sup>2</sup><https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-nirogacestat-desmoid-tumors>.

# BEST OVERALL RESPONSE (BOR) IN DeFi

## Double-Blind Phase (ITT Population)

BOR confirmed, n (%)	Niro (N=70 <sup>a</sup> )	Pbo (N=72)
Complete response (CR)	5 (7)	0
Partial response (PR)	24 (34)	6 (8)
Stable disease (SD)	35 (50)	55 (76)
Progressive disease (PD)	1 (1)	10 (14)
Not evaluable	4 (6)	1 (1)

Total exposure to niro in patients with SD was approximately half of those who achieved PR or CR.<sup>b</sup>

	Niro (n=35)	Pbo (n=55)
<b>Baseline Characteristics</b>		
Female, n (%)	21 (60)	36 (65)
Age, median (range), y	34 (18–64)	34 (18–76)
<b>DT treatment status, n (%)</b>		
Refractory	22 (63)	44 (80)
Treatment naïve	7 (20)	8 (15)
Recurrent	6 (17)	3 (5)

BOR, best overall response; DT, desmoid tumor; ITT, intent to treat; niro, nirogacestat; pbo, placebo.

<sup>a</sup>One patient discontinued before receiving niro. <sup>b</sup>Exposure defined as total number of equivalent completed cycles.

# PROs: Pts WITH STABLE DISEASE (BOR)

BPI-SF

## Brief Pain Inventory-Short Form

- Average pain intensity: worst pain<sup>a,b</sup>

GODDESS<sup>®</sup>

## Gounder/Desmoid Tumor Research Foundation Desmoid Symptom/Impact Scale

- Total symptom score (DT Symptom Scale)<sup>b</sup>
- Physical functioning domain (DT Impact Scale)<sup>c</sup>

EORTC  
QLQ-C30

## European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30<sup>d</sup>

- Physical functioning
- Role functioning
- Overall QoL

**Collected at screening/baseline & monthly; data shown for baseline & monthly from cycle 2–23  
(change from baseline at cycle 10 = key secondary endpoint)**

BOR, best overall response; DT, desmoid tumor; PRO, patient-reported outcome; pts, patients; QoL, quality of life.

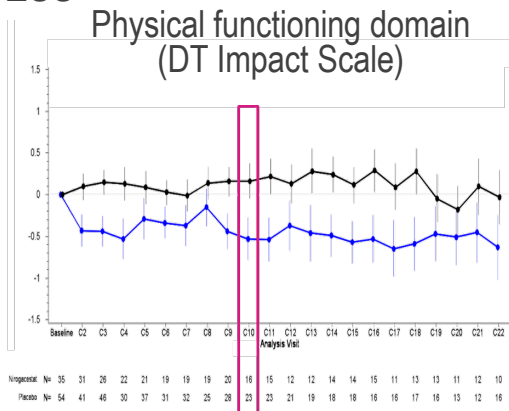
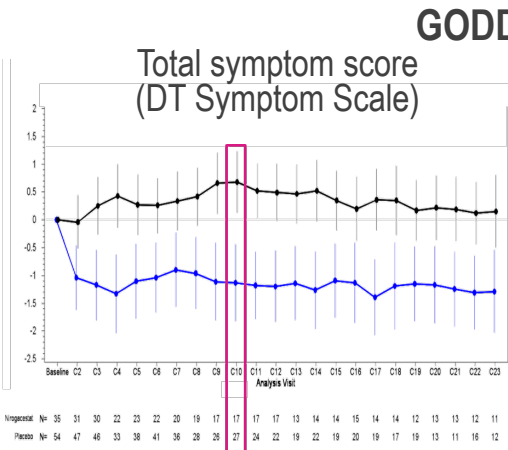
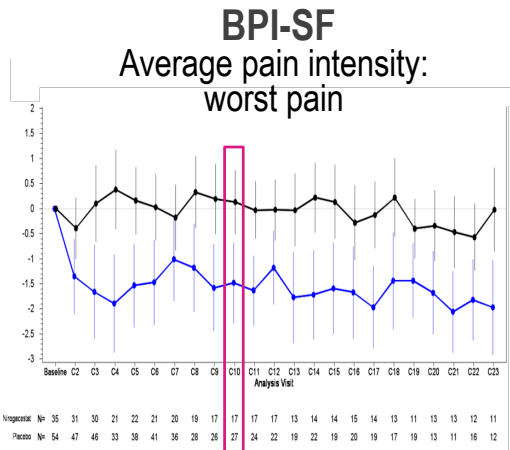
<sup>a</sup>Up to 7-day average of BPI-SF question #3: Worst pain in last 24 hours. <sup>b</sup>Utilizing an 11-point numeric rating scale. <sup>c</sup>Utilizing an 11-point numeric rating scale for severity or a 5-point Likert for frequency (7-day recall). <sup>d</sup>Each of the 30 questions on a 4-point scale (7-day recall).

# Pts WITH STABLE DISEASE RECIST v1.1 (BOR)

Change from Baseline in BPI-SF and GODDESS PROs

● Nirogacestat  
● Placebo

CfB by treatment cycle,  
LSMean (95% CI)



Improve

CfB at cycle 10, LSmMean (SE)

<b>Niro (n=35)</b>	-1.48 (0.40)	-1.13 (0.35)	-0.53 (0.12)
<b>Pbo (n=55)</b>	0.13 (0.32)	0.68 (0.28)	0.16 (0.10)
<b>Δ</b>	-1.62	-1.81	-0.69
<b>P-value</b>	<.001	<.001	<.001

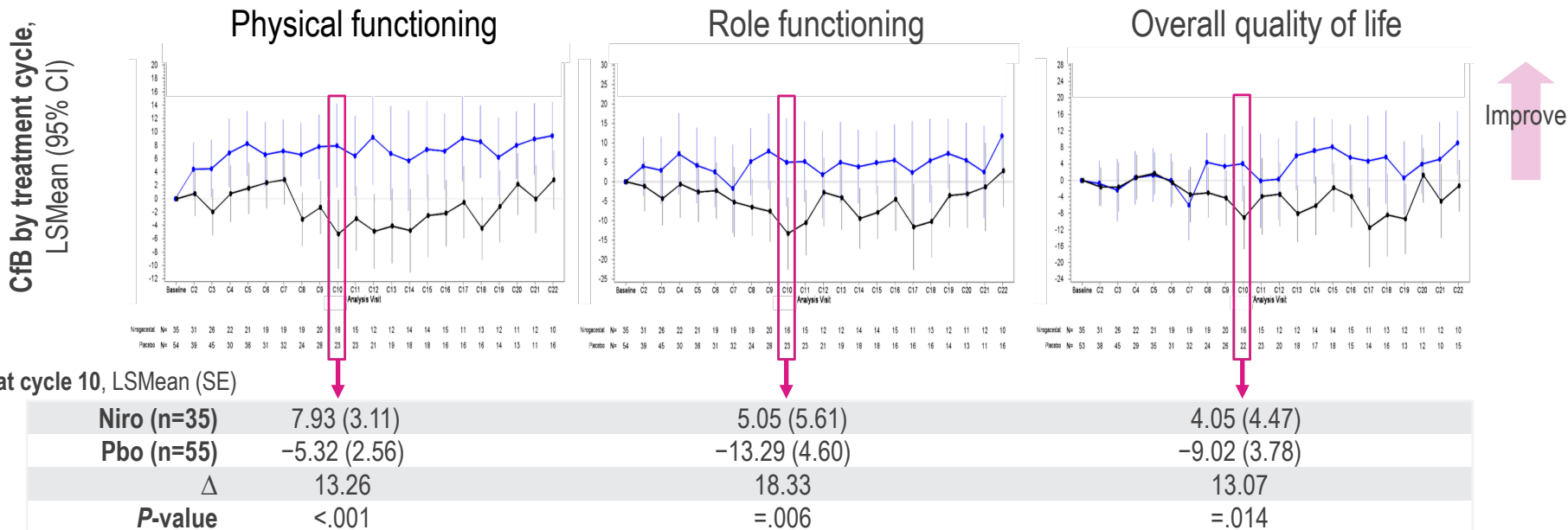
## Greater improvement from baseline with niro vs pbo

BOR, best overall response; BPI-SF, Brief Pain Inventory-Short Form; CfB, change from baseline; CI, confidence interval; DT, desmoid tumor; GODDESS, Gounder/Desmoid Tumor Research Foundation Desmoid Symptom/Impact Scale; LS, least squares; niro, nirogacestat; pbo, placebo; PRO, patient-reported outcome; pts, patients; SD, stable disease; SE, standard error.

# Pts WITH STABLE DISEASE RECIST v1.1 (BOR)

Change from Baseline in EORTC QLQ-C30 PROs

● Nirogacestat  
● Placebo



## Greater improvement from baseline with niro vs pbo

BOR, best overall response; CfB, change from baseline; CI, confidence interval; DT, desmoid tumor; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; LS, least squares; niro, nirogacestat; pbo, placebo; PRO, patient-reported outcome; pts, patients; SE, standard error.



# CONCLUSIONS: POST HOC ANALYSIS OF DeFi STUDY

- ◆ Nirogacestat-treated patients with stable disease as best overall response by RECIST v1.1 had **significant and clinically meaningful improvement in PROs** compared with placebo-treated patients, despite not achieving CR/PR
  - PROs included: pain, DT-specific symptom burden, physical functioning, role functioning, and overall quality of life
- ◆ Improvements were observed **early and were maintained throughout the double-blind study**

CR, complete response; DT, desmoid tumor; PR, partial response; PRO, patient-reported outcome; RECIST, Response Evaluation Criteria in Solid Tumors.

# ACKNOWLEDGEMENTS

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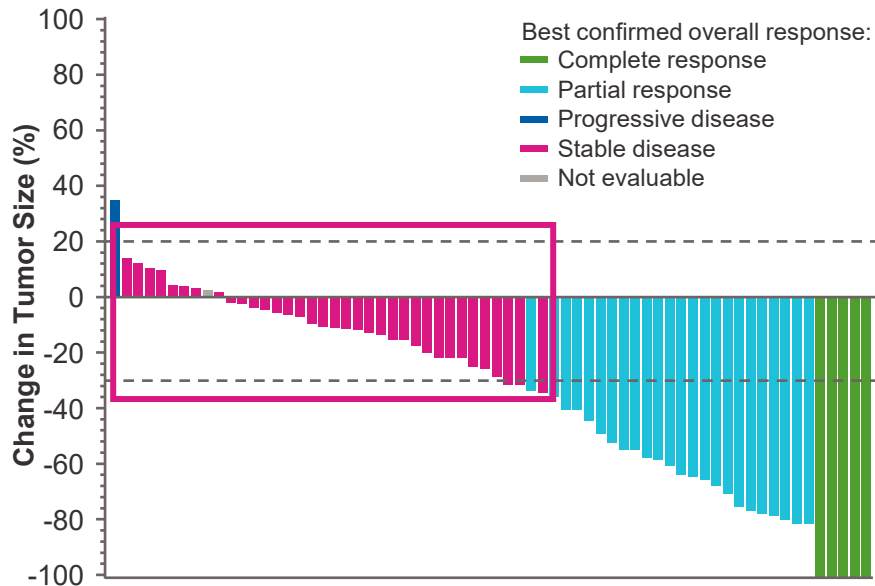
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# BACKUP

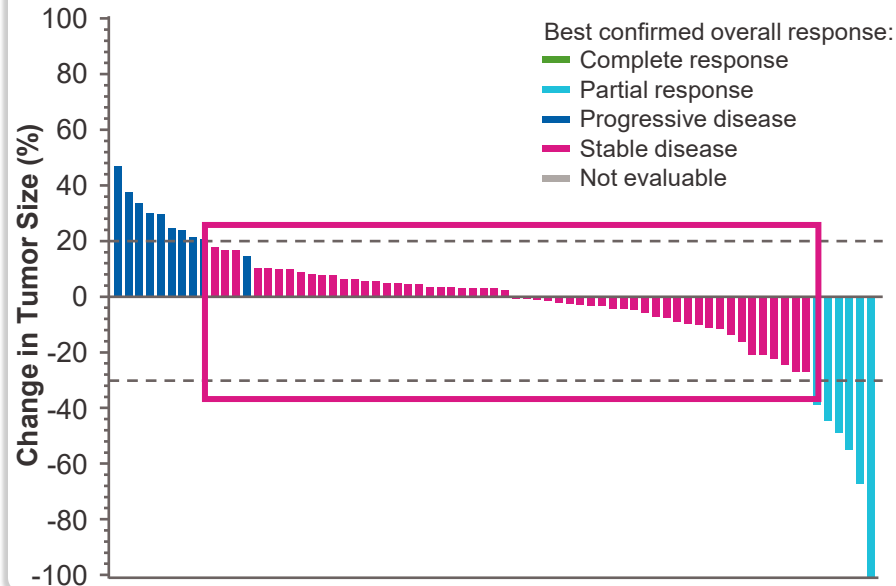


# BEST PERCENT CHANGE AT ANY TIME POINT FROM BASELINE IN TUMOR SIZE BY RECIST v1.1

## Nirogacestat



## Placebo



Best percent change values are averaged between 2 blinded independent reviewers unless a reader was selected for adjudication, in which case only the adjudicated value is presented. RECIST, Response Evaluation Criteria in Solid Tumors.

Adapted from Gounder M, et al. *N Engl J Med.* 2023;388(10):898-912.