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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, Bluprint, 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**[1]
  - 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**[1,2]**:**
  - Pain and DT symptom burden
  - Functioning with daily activities
  - Overall QoL

DT, desmoid tumor; PROs, patient-reported outcomes; QoL, quality of life.
[1]Bektas M, et al. *Adv Ther*. 2023;40(9):3697-3722. [2]Gounder MM et al. *Cancer*. 2020;126(3):531-539.

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NIROGACESTAT AND THE PHASE 3 DeFi STUDY

- **Nirogacestat,** selective gamma secretase inhibitor[1]
  - First treatment approved in the United States for adults with progressing DT[2]

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*≤.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. [a]Datacut: 07Apr2022.

[1]Gounder MM, et al. *N Engl J Med*. 2023;388(10):898-912. [2]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[a])	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.[b]

	Niro (n=35)	Pbo (n=55)
Baseline Characteristics		
Female, n (%)	21 (60)	36 (65)
Age, median (range), y	34 (18–64)	34 (18–76)
DT treatment status, n (%)		
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.
[a]One patient discontinued before receiving niro. [b]Exposure defined as total number of equivalent completed cycles.

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PROs: Pts WITH STABLE DISEASE (BOR)

BPI-SF

Brief Pain Inventory-Short Form

- Average pain intensity: worst pain[a,b]

GODDESS®

Gounder/Desmoid Tumor Research Foundation Desmoid Symptom/Impact Scale

- Total symptom score (DT Symptom Scale)[b]
- Physical functioning domain (DT Impact Scale)[c]

EORTC QLQ-C30

European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30[d]

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

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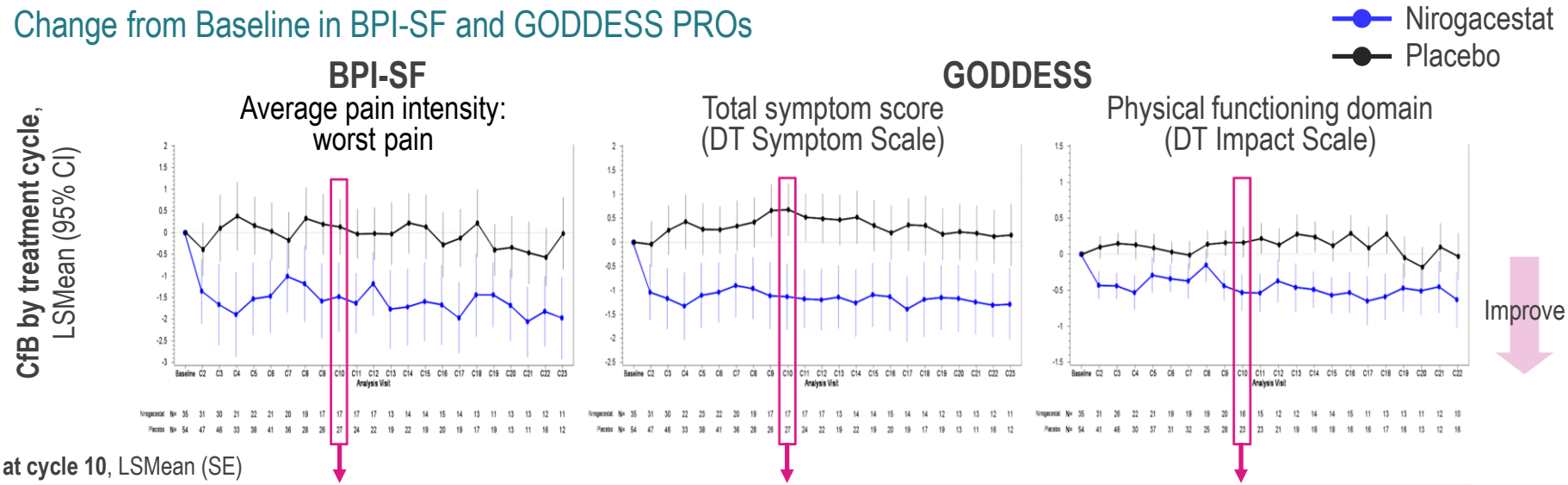
Pts WITH STABLE DISEASE RECIST v1.1 (BOR)

Change from Baseline in BPI-SF and GODDESS PROs



CfB at cycle 10, LSMean (SE)

	Average pain intensity: worst pain	Total symptom score (DT Symptom Scale)	Physical functioning domain (DT Impact Scale)
Niro (n=35)	−1.48 (0.40)	−1.13 (0.35)	−0.53 (0.12)
Pbo (n=55)	0.13 (0.32)	0.68 (0.28)	0.16 (0.10)
Δ	−1.62	−1.81	−0.69
***P*-value**	<.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.

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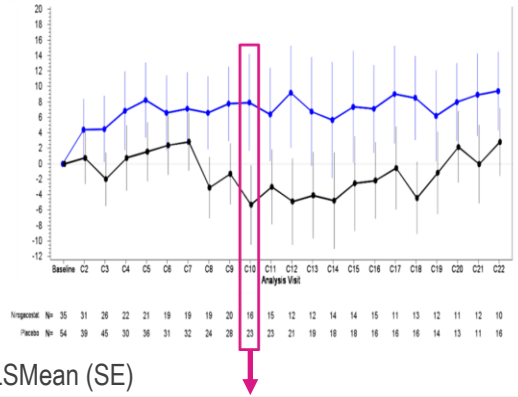
Pts WITH STABLE DISEASE RECIST v1.1 (BOR)

Change from Baseline in EORTC QLQ-C30 PROs

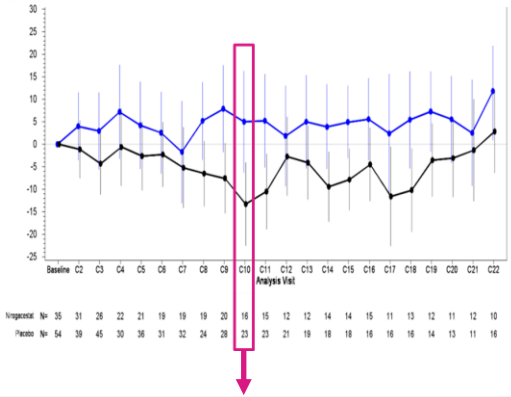
Nirogacestat
Placebo

CfB by treatment cycle, LSMean (95% CI)

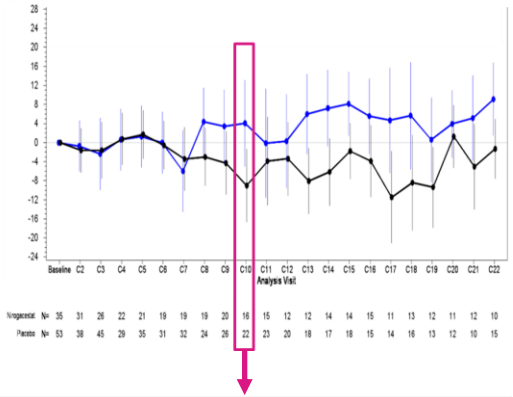
Physical functioning



Role functioning



Overall quality of life



Improve

CfB at cycle 10, LSMean (SE)

Niro (n=35)	7.93 (3.11)	5.05 (5.61)	4.05 (4.47)
Pbo (n=55)	−5.32 (2.56)	−13.29 (4.60)	−9.02 (3.78)
Δ	13.26	18.33	13.07
***P*-value**	<.001	=.006	=.014

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.

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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.

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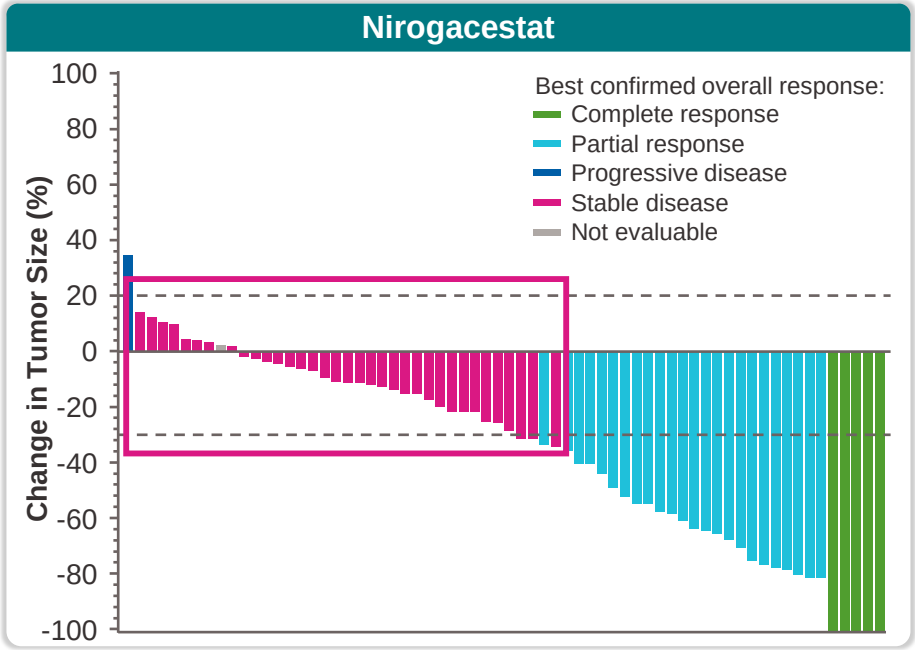
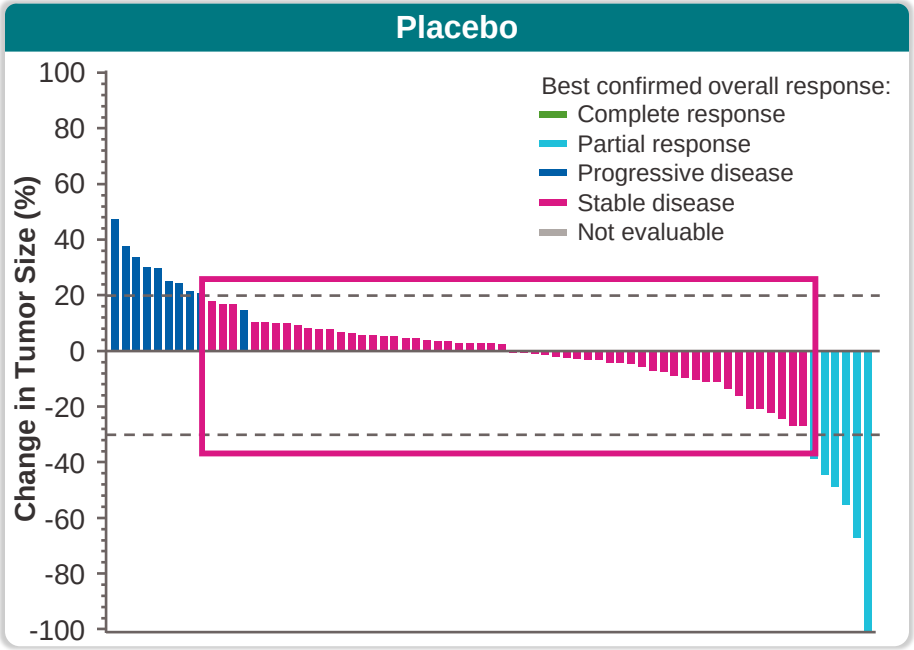
BACKUP

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





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.

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