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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*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.
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 (\(P\leq.01\) 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. Datacut: 07Apr2022.

**BEST OVERALL RESPONSE (BOR) IN DeFi**

Double-Blind Phase (ITT Population)

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

**Baseline Characteristics**

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

*Total exposure to niro in patients with SD was approximately half of those who achieved PR or CR.*

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

GODDESS®
Gounder/Desmoid Tumor Research Foundation Desmoid Symptom/Impact Scale
- Total symptom score (DT Symptom Scale)
- Physical functioning domain (DT Impact Scale)

EORTC QLQ-C30
European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30
- 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.

*Up to 7-day average of BPI-SF question #3: Worst pain in last 24 hours. *Utilizing an 11-point numeric rating scale. *Utilizing an 11-point numeric rating scale for severity or a 5-point Likert for frequency (7-day recall). *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

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**BPI-SF**

Average pain intensity: worst pain

<table>
<thead>
<tr>
<th>Treatment</th>
<th>LSMean (SE)</th>
<th>Pbo (n=55)</th>
<th>0.13 (0.32)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Niro</strong> (n=35)</td>
<td>-1.48 (0.40)</td>
<td>-1.13 (0.35)</td>
<td>-0.53 (0.12)</td>
</tr>
</tbody>
</table>

**GODDESS**

Total symptom score (DT Symptom Scale)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>LSMean (95% CI)</th>
<th>Pbo (n=55)</th>
<th>Placebo (n=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Niro</strong> (n=35)</td>
<td>-1.13 (0.35)</td>
<td>0.68 (0.28)</td>
<td>0.16 (0.10)</td>
</tr>
</tbody>
</table>

**Physical functioning domain (DT Impact Scale)**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>LSMean (95% CI)</th>
<th>Pbo (n=55)</th>
<th>Placebo (n=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Niro</strong> (n=35)</td>
<td>-0.53 (0.12)</td>
<td>0.16 (0.10)</td>
<td>.69 (0.10)</td>
</tr>
</tbody>
</table>

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

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<table>
<thead>
<tr>
<th>Treatment</th>
<th>Physical functioning</th>
<th>Role functioning</th>
<th>Overall quality of life</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Niro (n=35)</strong></td>
<td>7.93 (3.11)</td>
<td>5.05 (5.61)</td>
<td>4.05 (4.47)</td>
</tr>
<tr>
<td><strong>Pbo (n=55)</strong></td>
<td>−5.32 (2.56)</td>
<td>−13.29 (4.60)</td>
<td>−9.02 (3.78)</td>
</tr>
<tr>
<td><strong>Δ</strong></td>
<td>13.26</td>
<td>18.33</td>
<td>13.07</td>
</tr>
<tr>
<td><strong>P-value</strong></td>
<td>&lt;.001</td>
<td>.006</td>
<td>.014</td>
</tr>
</tbody>
</table>

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.

Greater improvement from baseline with niro vs pbo
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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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.