SGO 50th Annual Meeting on Women’s Cancer

Hawaii Five-O

Honolulu • March 16-19, 2019
Time without symptoms or toxicity in patients with recurrent ovarian cancer receiving niraparib maintenance treatment versus placebo: A TWiST analysis of the ENGOT-OV16/NOVA trial

Disclosures

• Ursula A. Matulonis:
  • Chief, Division of Gynecologic Oncology
  • Received personal fees to provide advice and consult for Merck, Clovis Oncology, Geneos, Mersana, and Immunogen outside of the submitted work.
Identify the delay in disease progression not offset by toxic effects due to nausea, vomiting or fatigue

- **Objective:**
  - Estimate the difference in time without symptoms or toxicity (TWiST) between treatment with maintenance niraparib or placebo in the ENGOT-OV16/NOVA trial

Data were sourced from the ENGOT-OV16/NOVA trial

ENGOT-OV16/NOVA trial (NCT01847274)

- Randomized controlled phase III trial
- Recurrent ovarian cancer patients
- Niraparib was assessed for safety and efficacy compared to the placebo in both the gBRCAmut and non-gBRCAmut cohorts
- Primary endpoint – progression-free survival (PFS)
Identify the delay in disease progression not offset by toxic effects due to nausea, vomiting or fatigue

• Topline Results:
  • Treatment with maintenance niraparib significantly delayed disease progression compared to placebo - Mirza et al. 2016
    - gBRCAmut; 21.0 vs. 5.5 months, non-gBRCAmut; 9.3 vs. 3.9 months
  • Quality of life (remained stable through niraparib treatment and pre-progression period - Oza et al. 2018
    - QOL parameters tested: EQ-5D-5L, EQ-5D-5L-VAS, and FOSI

PFS was extrapolated over 20-years to estimate the expected benefits beyond the length of the ENGOT-OV16/NOVA trial

- Survival curves were used to extrapolate PFS ENGOT-OV16/NOVA data for niraparib and placebo over 20-years for both the gBRCAmut and non-gBRCAmut cohorts
- The 20-year period was based on ovarian cancer clinical expert opinion, and this approach has been accepted in 2 previous health technology appraisal submissions

### Step 1: Mean PFS was calculated as the area under the curve and is represented in years

Time with toxicity was estimated from the number of days patients experienced toxic effects due to grade ≥2 nausea, vomiting or fatigue in the ENGOT-OV16/NOVA trial

• Time with toxicity (TOX) was estimated from the number of days patients experienced grade ≥2 symptomatic adverse events (AEs):
  • Nausea, vomiting and fatigue
  • AEs were included post randomization and prior to disease progression
• Using this data toxicity Kaplan-Meier curves were estimated for both the gBRCAmut and non-gBRCAmut cohorts

Step 2: Mean TOX was calculated as the area under the curve and is represented in years
TWiST was calculated as PFS without toxicity due to grade ≥2 symptomatic adverse events: nausea, vomiting and fatigue.

TWiST is an established methodology that partitions PFS into two health states:

1. Time with toxicity (TOX)

2. Time without symptoms (i.e. progression) or toxicity (TWiST)
TWiST was calculated as PFS without toxicity due to grade ≥2 symptomatic adverse events: nausea, vomiting and fatigue.

TWiST is an established methodology that partitions PFS into two health states:

1. Time with toxicity (TOX)
2. Time without symptoms (i.e. progression) or toxicity (TWiST)

Mean TWiST = mean PFS – mean TOX
gBRCAmut cohort treated with niraparib experienced greater PFS without toxicity due to nausea, vomiting or fatigue.

<table>
<thead>
<tr>
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<th>Mean PFS (95% CI, SE)</th>
<th>Mean TOX (95% CI, SE)</th>
<th>Mean TWiST</th>
<th>Incremental TWiST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Niraparib</td>
<td>4.14 years (2.20, 7.04;1.25)</td>
<td>0.31 years (0.19, 0.44; 0.06)</td>
<td>3.83 years</td>
<td>2.95 years</td>
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<tr>
<td>Placebo</td>
<td>0.91 years (0.51, 1.90; 0.35)</td>
<td>0.03 years (0.01, 0.06; 0.01)</td>
<td>0.88 years</td>
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</table>
Non-gBRCAmut cohort treated with niraparib experienced greater PFS without toxicity due to nausea, vomiting or fatigue.
Patients treated with niraparib in the ENGOT-OV16/NOVA trial experienced a mean TWiST benefit compared to placebo

- This TWiST benefit means that patients treated with niraparib experienced more progression-free time without symptoms or toxicities due to nausea, vomiting or fatigue compared to placebo
Acknowledgments

We thank the 553 patients and their families for participating in this trial.