Roginolisib, an Oral, Highly Selective and AllostERIC Modulator of Phosphoinositide 3-kinase Inhibitor delta (PI3Kδ) in Patients with Uveal Melanoma and Advanced Cancers

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Abstract #9597: Roginolisib, an Oral, Highly Selective and AllostERIC Modulator of Phosphoinositide 3-kinase Inhibitor delta (PI3Kδ) in Patients with Uveal Melanoma and Advanced Cancers

**BACKGROUND**

- PI3Kδ expression is correlated with immune suppressive immune cells, such as Treg cells.
- Highly selective PI3Kδ inhibition results in blocking tumour-cell intrinsic and extrinsic pathways.
- Roginolisib (formerly IOA-244) has a unique mechanism of action as an allostERIC modulator and a highly selective PI3Kδ inhibitor.

**OBJECTIVES**

- Primary: Safety and tolerability of escalating doses of IOA-244 to the predicted biological effective dose (BED).
- Secondary: To assess the pharmacokinetic (PK) profile.
- Characterize pharmacodynamics (PD) effect as determined by inhibition of COX3 expression on basophils in response to IOA-244.
- To document antitumor activity, including overall response rate (ORR), duration of response (DoR), progression free survival (PFS) and overall survival (OS).

**METHODS**

- Design: 3+3 cohort dose escalation
- Patients: Eligibility
- Minimum age of 18 years with the following:
  - Performance status of ≤2 on the ECOG scale
  - Histological or cytological evidence of a diagnosis of cancer that is advanced and/or metastatic disease
  - Adequate organ functioning (NHL for mesothelioma, cutaneous, and uveal melanoma or non-Hodgkin lymphoma follicular lymphoma (NHL-FL))
  - Adequate organ functioning
- Assessments:
  - Toxicity: graded according to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0
  - Standard laboratory hematology and chemistry
  - RECIST 1.1: based evaluation (ORR) – exploratory studies with radiomics were conducted

**RESULTS**

**Table 1: Demographics and Baseline Characteristics**

<table>
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<tr>
<th>Characteristic</th>
<th>Overall</th>
<th>SD mg</th>
<th>MD mg</th>
<th>MD mg</th>
<th>MD mg</th>
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<th>Overall</th>
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<td>Age (years)</td>
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<td>58 (30-74)</td>
<td>76 (54-81)</td>
<td>62 (44-93)</td>
<td>74 (59-94)</td>
<td>75 (49-95)</td>
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<tr>
<td>Gender</td>
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<td>35 (57)</td>
<td>47 (69)</td>
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<td>Race</td>
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<td>37 (58)</td>
<td>38 (57)</td>
<td>40 (58)</td>
<td>40 (57)</td>
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<td>Primary diagnosis</td>
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<td>18 (30)</td>
<td>23 (35)</td>
<td>21 (30)</td>
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<td>Metastatic status</td>
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<td>26 (39)</td>
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</table>

**Figure 1: Safety of 40 mg (A) and Drug-related (B)**

**Figure 2: Time on roginolisib for UM patients -60% treated beyond 6 months**

- The CTCAE 4.03 (Grade 2 and above) are shown for each patient group.
- The top portion of each bar indicates the number of patients treated at each dose level. The bottom portion of each bar indicates the number of patients treated at each dose level.

**Figure 3: Spider plots for uveal melanoma patients**

**Figure 4: Changes in total tumor volumes using radiomics assessment in UM patients per SD and PD at Week 16 (Cycle 5 Day 1)**

- The total tumor volume (TUMOUR ACTIVITY) was compared across different treatment regimens.
- The comparison was done using RECIST 1.1 at week 16.
- The comparison was done using RECIST 1.1 at week 26.

**Figure 5: Changes in spleen volumes using radiomics assessment in UM patients per SD and PD at Week 16 (Cycle 5 Day 1)**

- The comparison was done using RECIST 1.1 at week 26.
- The comparison was done using RECIST 1.1 at week 26.

**Figure 6: Overall Survival (Kaplan-Meier, KM, Plots) for all uveal melanoma patients**

- The KM plots were used to estimate the survival rate.
- The KM plots were used to estimate the survival rate.

**Figure 7: KM Plots for uveal melanoma patients With SD and PD at Week 16 (by RECIST 1.1 response)**

- The KM plots were used to estimate the survival rate.
- The KM plots were used to estimate the survival rate.

**Figure 8: Patients treated with roginolisib**

- The KM plots were used to estimate the survival rate.
- The KM plots were used to estimate the survival rate.

**CONCLUSIONS**

- Roginolisib has a low toxicity profile (<5 Grade 3/4), including when given every 4 weeks at 80 mg QD.
- At Week 16 (~38.8 mo), patients can be divided into two groups: (1) with SD (13/29; 45%) and PD (16/29; 55%).
- Patients with SD at Week 16 have a median OS of 28.5 months, while patients with PD at Week 16 have a median OS of 10.9 months.
- Roginolisib’s results and evaluation of Total Tumor Burden evolution, suggest that patients with Stable Disease (SD) at Week 16 experience better overall tumour growth control over their previously progressing disease after initiating treatment with roginolisib.