9110:
PH I/II STUDY OF ORAL SELECTIVE AXL INHIBITOR BEMCENTINIB (BGB324) IN COMBINATION WITH ERLOTINIB IN PATIENTS WITH EGFRm NSCLC: END OF TRIAL UPDATE

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- James Strauss - Mary Crowley Cancer Research Unit, Dallas, TX/USA
- Jorge Nieva - USC Norris Comprehensive Cancer Center, Los Angeles, CA/USA
- Julio Peguero - Oncology Consultants, Houston/USA
- Kathryn Gold - UC San Diego Health, LaJolla/USA
- Melissa L. Johnson - Sarah Cannon Research Institute, Nashville, TN/USA
- Wael A.Harb - Horizon Oncology Center, Lafayette, IN/USA
Study rationale and design

**AXL Biology and Bemcentinib Mode of Action**

- AXL is a member of the Tyro3, AXL, Mer (TAM) family of receptor tyrosine kinases, activated by Growth Arrest Specific Factor (Gas6)
- Bemcentinib is a first-in-class highly selective, potent, and orally bioavailable, small molecule AXL kinase inhibitor
- AXL is a negative prognostic factor for many cancers including NSCLC
- Bypass signaling by AXL is a significant mechanism for acquired resistance to EGFR-targeting therapies such as erlotinib
- Inhibition of AXL suppresses and reverses somatic acquired resistance to EGFR-targeting therapies
- AXL drives tumor EMT, resistance to cytotoxic lymphocyte-mediated cell killing and innate immune suppression and these are reversed by treatment with bemcentinib

- AXL IHC high (n=29)
- AXL IHC low (n=59)

**Bemcentinib prevents resistance to erlotinib in vivo**

**BGBC004 : Ph I/II Study of Oral Selective AXL Inhibitor Bemcentinib in Combination with Erlotinib in Patients with EGFRm NSCLC**

**Run-in Cohort**
Single agent BGB324 in NSCLC patients with progression after prior therapy (n=8)

**ARM A (Dose Escalation) – BGB324 + erlotinib**
Patients with ≥ 6 weeks of erlotinib 150mg daily (n=8)

Dose escalate until MTD / RP2D
Minimum of 6 patients at MTD / RP2D

**ARM B (Erlotinib Progression)**
Patients with EGFR mutation, T790M-neg* with progression on erlotinib
Daily BGB324 + erlotinib (n=11)

*patients who have previously been treated with a T790M inhibitor i.e., osimertinib and who have progressed will not require T790M testing

**ARM C (First-line Erlotinib Combo)**
Patients with EGFR mutation with ≥ 4 cycles of erlotinib in first-line setting
Daily BGB324 + erlotinib (n = 13)

Endpoints: Safety, tolerability pharmacokinetics and preliminary efficacy
Exploratory: Pharmacodynamics, sAXL expression and blood biomarkers

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**Presented By:** Dr. Lauren Averett Byers

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Patient A

- A 68-year-old white female, diagnosed with stage IV adenocarcinoma of the lung and EGFR mutation positive (exon 21 insertion - L858R substitution)
- Received 1 line of prior treatment (Dacomitinib as 1L treatment with PR as best response)
- Received bemcentinib + erlotinib for 1174 days (39.1 months) with best response on trial as PR
Phase II: Previously treated patients with activating EGFR mutation driven NSCLC actively progressing on an approved EGFR inhibitor (Arm B)

**Patient Characteristics**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Arm B (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (range)</td>
<td>63 (49-78)</td>
</tr>
<tr>
<td>Median ECOG score (range)</td>
<td>1 (0-1)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>7 (64)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Asian (%)</td>
<td>6 (55)</td>
</tr>
<tr>
<td>Caucasian (%)</td>
<td>5 (45)</td>
</tr>
<tr>
<td>Type of EGFR mutation</td>
<td></td>
</tr>
<tr>
<td>Exon 21 insertion (%)</td>
<td>4 (36)</td>
</tr>
<tr>
<td>Exon 19 deletion (%)</td>
<td>6 (54)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (9)</td>
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<tr>
<td>Best response to previous Erlotinib treatment</td>
<td></td>
</tr>
<tr>
<td>PR (%)</td>
<td>6 (54.5)</td>
</tr>
<tr>
<td>SD (%)</td>
<td>3 (27.2)</td>
</tr>
<tr>
<td>PD (%)</td>
<td>2 (18.1)</td>
</tr>
<tr>
<td>Undetermined</td>
<td>0</td>
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</tbody>
</table>

**Time on treatment (Bemcentinib + Erlotinib combination) for patients in Arm B (n=11)**

**Patient B**
- 52-year-old white male, diagnosed with stage IV adenocarcinoma of the lung with mets in liver, pleura and lymph nodes
- EGFR mutation positive (exon 21 insertion), T790m negative
- 3 prior lines (erlotinib, nivolumab and docetaxel) prior to enrolment
- Received bemcentinib + erlotinib for 356 days (11.9 months) with PR as a best response to treatment despite progression on erlotinib immediately prior

**Patient C**
- 62-year-old white female, diagnosed with stage IV adenocarcinoma of the lung
- Received three prior lines of treatment prior to enrolment including erlotinib in both adjuvant and metastatic setting with no response to either treatment
- EGFR mutation positive (exon 21 insertion), T790m negative
- Received bemcentinib + erlotinib for 180 days (6.1 months) with SD as best response to the treatment
Phase II: 1L patients with activating EGFR mutation driven NSCLC on erlotinib with stable disease or partial response (Arm C)

**Patient Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Arm C (n=13)</th>
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<tbody>
<tr>
<td>Median age (range)</td>
<td>61 (57-67)</td>
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<tr>
<td>Median ECOG score (range)</td>
<td>1 (0-1)</td>
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<tr>
<td>Female (%)</td>
<td>5 (63)</td>
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**Ethnicity**

- Asian (%) 1 (13)
- Caucasian (%) 5 (63)

**Type of EGFR mutation**

- Exon 21 insertion (%) 4 (31)
- Exon 19 deletion (%) 8 (62)
- Unknown (%) 1 (8)

**Best response to previous Erlotinib treatment**

- PR (%) 5 (38.4)
- SD (%) 5 (38.4)
- PD (%) 0
- Undetermined 3 (23.2)

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**Time on treatment (Bemcentinib + Erlotinib combination) for patients in Arm C (n=13)**

- **Patient D**
  - 65-year-old Asian female, diagnosed with stage IV adenocarcinoma of the lung
  - EGFR mutation positive (exon 19 deletion)
  - Received prior erlotinib for 12 months and achieved PR
  - Enrolled and continued bemcentinib + erlotinib for 1400 days (46.8 months)
  - Achieved SD as best response with additional 10% deepening of response (following ongoing prior PR) and remains on treatment

- **Patient E**
  - 65-year-old white female, diagnosed with stage IV adenocarcinoma of the lung
  - EGFR mutation positive (exon 21 insertion - L858R)
  - Received prior erlotinib for 9 months with SD
  - Enrolled and continued bemcentinib + erlotinib for 1042 days (34.7 months)
  - Achieved SD as best response with additional 25% deepening of response (following ongoing prior SD) and remains on treatment

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**Data cut off = 31-Mar-2021**
## Conclusions

- Bemcentinib 200mg daily (RP2D) in combination with erlotinib 150mg was well tolerated over extended periods of time (46 months for longest ongoing patient).

- The erlotinib + bemcentinib combination led to disease stabilisation and durable tumour responses in a proportion of patients who had previously progressed on EGFR targeted therapy and who were negative for the T790M resistance mutation.

- In patients who were responding to 1L erlotinib (either SD or PR), addition of bemcentinib led to further deepening of responses and prolonged duration of responses beyond 30 months in 4 out of 13 patients.

- At the time of data cut-off, 2 patients are still ongoing in the study beyond 34 months of treatment (Any ongoing patient at the time of study closure, who wishes to receive study treatment, will be offered the drug via expanded access program)

### TRAEs (Grade ≥ 3) reported by Preferred Term in ≥5% of patients by decreasing order of frequency (N=40)

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<thead>
<tr>
<th>Preferred Term</th>
<th>N</th>
<th>%</th>
<th>E</th>
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<tr>
<td>Diarrhoea</td>
<td>11</td>
<td>28%</td>
<td>17</td>
</tr>
<tr>
<td>Fatigue</td>
<td>2</td>
<td>5%</td>
<td>2</td>
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<tr>
<td>Transaminases increased</td>
<td>2</td>
<td>5%</td>
<td>2</td>
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## Disclosures

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<th>Commercial Interest</th>
<th>Relationship(s)</th>
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## Acknowledgements

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<th>All BGBC004 study investigators</th>
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THANK YOU

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