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General AML

Phase II study of bemcentinib for AML

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Bemcentinib is a first-in-class, potent, small selective molecule inhibitor of AXL, which is a surface membrane protein overexpressed in up to half of acute myeloid leukemia (AML) cases.[1] It has exhibited anti-leukemic activity as monotherapy in patients with relapsed/refractory (R/R) AML.[2]

A phase I dose escalation and expansion study (NCT02488408) of bemcentinib monotherapy has previously been completed which identified the recommended phase II dose (RP2D) to be 200mg orally, daily (po/d).[2] The phase I portion also aimed to identify anti-leukemic activity.

The phase II portion was designed to investigate the safety and efficacy of bemcentinib in combination with low dose cytarabine (LDAC) or decitabine when administered to patients with R/R AML who were unfit for intensive chemotherapy. Results from the phase II portion of the study (BGBC003) were presented during a poster sessions at the American Society of Clinical Oncology (ASCO) meeting, and at the European Hematology Association (EHA) annual meeting, by Sonja Loges and colleagues. Secondary objectives included overall survival (OS) and exploratory biomarker analysis.[2,3]

Dosing schedule was as below:[2]

- Bemcentinib (200mg po/d) + LDAC, n= 11
- Bemcentinib (200mg po/d) + decitabine, n= 15

Patient characteristics: bemcentinib + LDAC arm[3]

- Ten patients were evaluable for assessment by bone marrow aspirate at cycle two, day one
  - Median age: 76 years (range; 66–83)
  - Poor cytogenetic risk profile: 60%
  - Median screen myeloblast count was 33% (3–96)
  - None of the nine evaluable patients were *FLT3*$^{+}$
  - Six patients had been previously treated
    - Relapsed: n= 3
    - Refractory: n= 3

Safety: bemcentinib + LDAC arm[3]

Treatment-related adverse events (TRAEs):

- Thirteen patients were dosed with bemcentinib + LDAC and were evaluable for safety
- Four patients experienced a TRAE (31%)
- Most common TRAEs:
- Anemia: 15%
- Diarrhea: 15%
- Two patients experienced TRAEs ≥ grade III
- Two patients experienced febrile neutropenia unrelated to study drug

Efficacy: bemcentinib + LDAC arm[3]

At a data cut-off of March 2019:

- Bemcentinib + LDAC arm (n= 10):[3]
  - Four patients (40%) achieved an objective response at cycle two, day one
    - Three patients achieved a complete response (CR) or CR with incomplete hematologic recovery (CRi)
    - One patient achieved a partial response (PR)
    - Two of these patients had *de novo* AML and two had been previously been treated (one refractory)
    - Three had unfavorable cytogenetics
    - Three were over the age of 75 years
    - Durable responses; n= 3 (3.5, 4.9 and 6.9 months, ongoing responses)
  - Stable disease (SD): 20% (2/10)[3]
    - Both patients were 76 years old
    - One of these patients had secondary AML and the other had relapsed disease
    - Durable SD; n= 2 (4.0 and 3.9 months, one ongoing)

Median progression-free survival (PFS) in the five patients with durable CRi or SD was reported to be 5 months (3.5–7.7) at the ASCO meeting.[2]

Efficacy: bemcentinib + decitabine arm[2]

- In the bemcentinib + decitabine arm (n= 11):
  - CRi after four or more cycles: 36% (4/11)
    - The four responders all had *de novo* AML
  - One further patient achieved durable SD lasting for five cycles

Conclusion

The authors concluded that bemcentinib, in combination with LDAC, provided durable responses in patients with *de novo* and R/R AML, as well as in elderly patients and those with poor-risk disease.[3] Treatment with bemcentinib with decitabine achieved fewer responses, and those that were observed occurred later.[2]

Regulatory approvals

Bemcentinib was recently approved for fast track designation by the United States (US) Food & Drug Administration. Currently bemcentinib is in expanded phase II trials in the US and Europe.[4]

References

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