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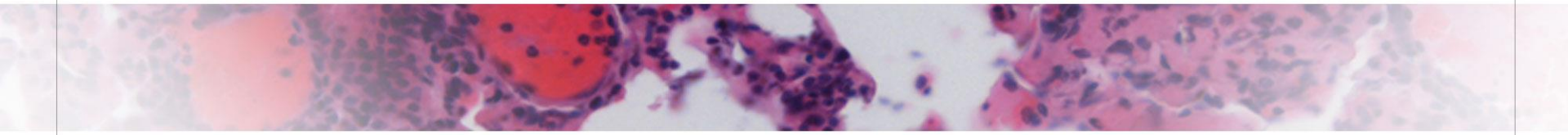

Biomarker-Driven Phase Ib Clinical Trial of OPB111077 in Acute Myeloid Leukemia Increases Overall Response Rates

Authors:

J Martinez-Lopez[1], P Montesinos[2], MP Martinez-Sanchez[1], Julian Gorrochategui[3], Jose-Luis Rojas[3], Daniel Primo[3], Juan Miguel Bergua[4], R Ayala[1], M Calbacho[1], Nieves Lopez-Muñoz[1], Evelyn Acuña-Cruz[2], Jose Antonio Pérez-Simón[5], Adolfo de la Fuente[6], Jaime Perez De Oteyza[7], Rebeca Rodriguez-Veiga[2]; Blanca Boluda[2]; Isabel Cano[2], Joan Ballesteros[3]

Institutions:

1. Hospital Universitario 12 de Octubre, Madrid; 2. Hospital Universitari i Politecnic La Fe, Valencia; 3. Vivia Biotech; 4 Hospital San Pedro de Alcántara, Cáceres; 5. Hospital Virgen del Rocío, Sevilla; 6. MD Anderson, Madrid; 7. Hospital Universitario Madrid Sanchinarro, Madrid.

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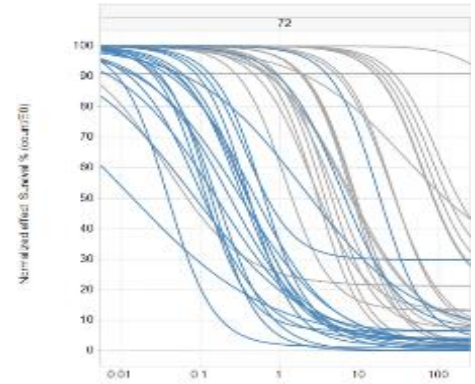
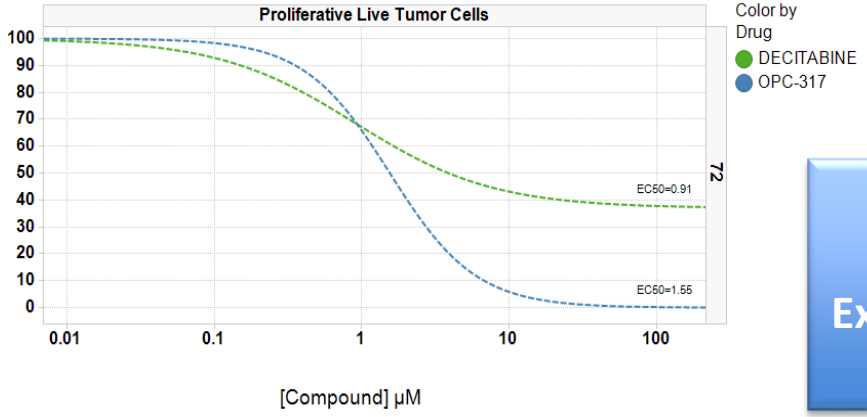
Ex Vivo Sensitivity Identified Potent Activity as an Anti-Proliferative Agent in AML



Activity by dose response curves

Very high interpatient variability

Proliferative >> Non-proliferative cells



Activity on proliferative AML cells is better than Decitabine

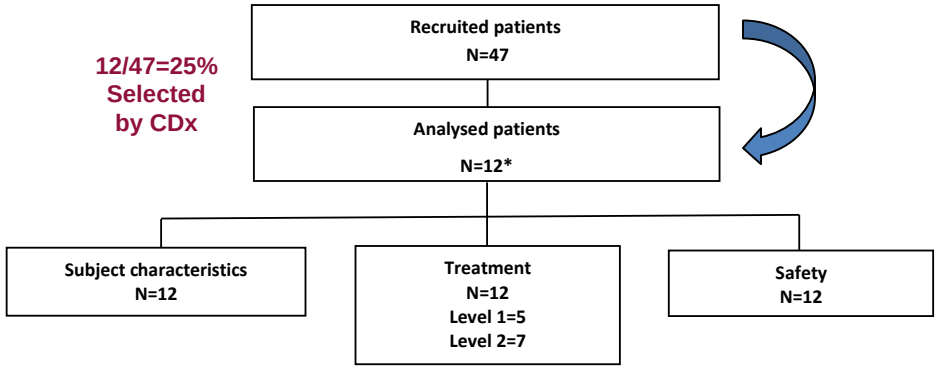
Launch Phase I.B IST using ex vivo sensitivity as CDx
Expect weak activity as Decitabine, best for combinations

Background

- OPB-111077 is a novel, oral, low-molecular-weight compound that inhibits STAT3 and mitochondrial electron transport.
- A prior Phase I trial on 145 patients from all tumor types gave only 1 partial response.
- A strong anti-proliferative activity was identified in Acute Myeloid Leukemia (AML) samples ex vivo.
- This new biomarker attempts to identify sensitive subpopulations in this phase Ib trial in AML patients.

Study design and objectives

- Phase Ib dose escalation clinical trial.
- Patients > 18 years old with high risk AML, ECOG ≤2 and adequate organ functions were selected for biomarker screening.
- Higher sensitivity to ex vivo biomarker (antiproliferative activity).
- OPB-111077 was administered orally once daily Two dose schemas were evaluated: 200 mg/day (DL1) and 250 mg/day (DL2).
- Dose limiting toxicities:
  - Any Grade ≥ 3 non-hematologic toxicity
  - Any unexpected non-tolerable grade II that requires delay beyond 1 week until recovery and evaluated during the first 28 days of treatment.



Results (1/3) Patient Characteristics

Characteristics	N (%)
➢ Number of patients	12
• DL1 (200 mg/d)	5 (41.7%)
• DL2 (250 mg/d)	7 (58.3%)
➢ Age (Years; Median/Range)	76.0 (72.0-79.0)
➢ Weight (kg; Median/Range)	69.0 (64.8-79.3)
➢ Sex	-
• Female	1 (8.3%)
• Male	11 (91.7%)

Characteristics	N (%)
➢ ECOG	-
• 0	5 (41.7%)
• 1	6 (50.0%)
• Unknown	1 (8.3%)
➢ Concomitant disease	1 (8.3%)
➢ Refractory	5 (41.7%)
➢ Median of relapses (Median/Range)	2 (1-6)
➢ Prior treatment lines (Median/Range)	2 (1-4)

Results (2/3) Safety / Discontinuations

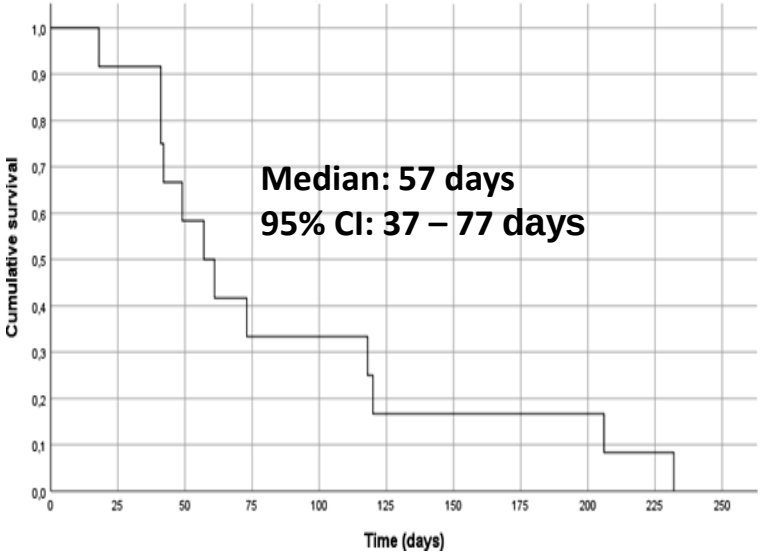
*Toxicities to OPB-111077	Nº patients	Grade
➢ DL1	1	-
• Vomiting	1	2
➢ DL2	2	-
• Vomiting	1	1
• Extrasystoles	1	2
• Nauseas	1	1
• Anorexia	1	1
• Diarrhoea	1	1
• Epigastric discomfort	1	1

Discontinuation	N (%)
➢ Disease Progression	6 (50.0%)
➢ Death (Respiratory infection)	1 (8.3%)
➢ Adverse event	2 (16.7%)
• Respiratory failure	1 (8.3%)
• Extrasystoles	1 (8.3%)
➢ Withdraw consent	1 (8.3%)
➢ Other reasons*	2 (16.7%)
• Clinical/Analytical worsening	1 (8.3%)
• Refractory	1 (8.3%)

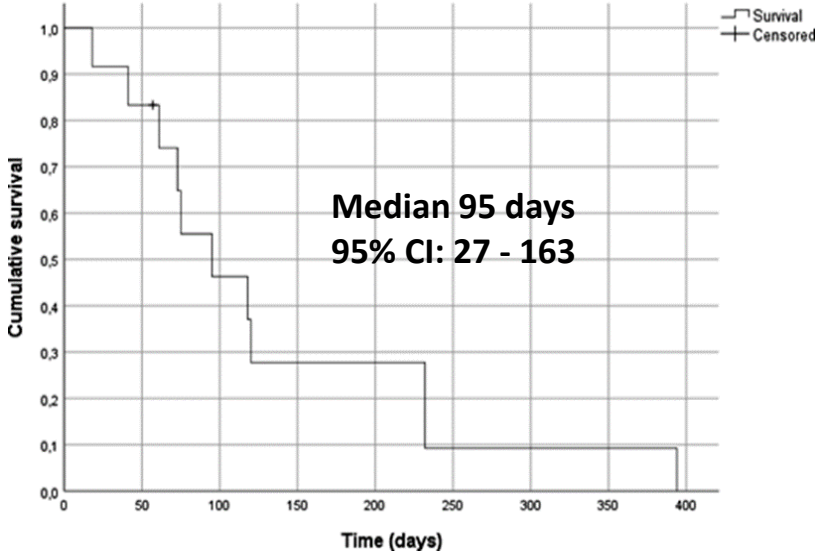
***No DLT was reported**

Results (3/3) PFS and OS

Progression Free Survival



Overall Survival



Over the 6 patients evaluable for efficacy, 3 of them achieved PR.

Median PFS for the 3 patients who achieve PR: 206 days (65 - 347).

Biomarker analysis

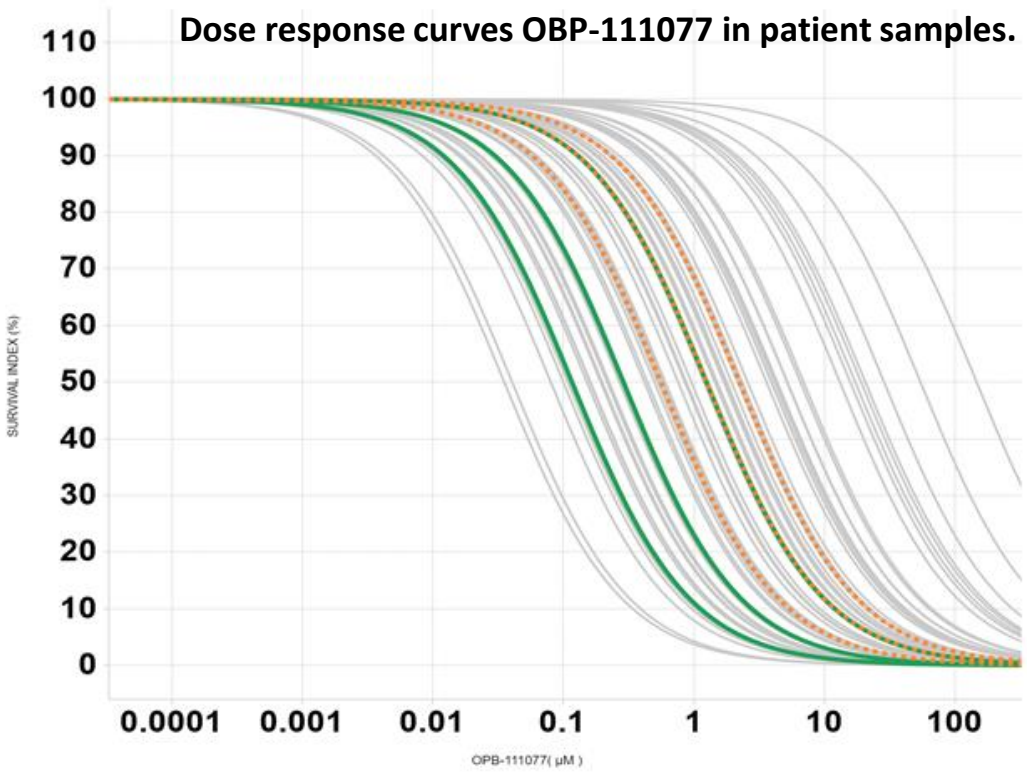


Figure shows the relative position of patients included in the study in the context of the overall population of samples considered to build up the mixed effect population pharmacodynamic model used to analyze samples results and define inclusion criteria.

In **green** those that correspond to patients who showed a positive response.

In **orange** those who failed.

Conclusions

- **OPB-111077 is generally well tolerated and has a manageable toxicity profile. The MTD was not reached.**
- **The 50% PR rate achieved by OPB-111077, albeit in a few patients, is substantially higher that the 0.7% (1/145) PR rate achieved in a prior phase I trial on all tumor types[1].**
- **This innovative Phase Ib design selecting patients using a biomarker may enable to rescue drug failures in the future.**

1. Tolcher A, Flaherty K, Shapiro GI et al. Oncologist. 2018, 23(6):658-e72

Acknowledgments

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