Treatment for infant Acute Lymphocytic Leukemia

MISSION

To boost chemotherapy sensitivity and improve prognosis of infant t(4;11) pro-B-ALL patients through the increase of HDAC7 expression.

SECTOR

Therapeutics

STAGE

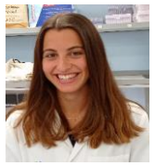
Preclinical assays

POTENTIAL INDICATIONS

- Infant t(4;11) pro-B-ALL with adverse prognosis
- Pro-B-ALL in adults with t(4;11)
- Other hematological malignancies (DLBCL…)

TEAM

Dr Maribel Parra
Principal investigator



Mar Gusi-Vives
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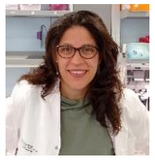

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COLLABORATORS

Interfant consortium

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Giovanni Cazzaniga (University of Milan, Italy)

Pablo Menéndez (IJC, Barcelona)

THE PROBLEM

- t(4;11)-rearranged pro-B-ALL is a highly aggressive subtype of pro-B-ALL associated with a 35% of survival rate
- t(4;11) pro-B-ALL patients present chemoresistance to current treatment and usually relapse
- No other therapeutic options are available for these patients, particularly for infants under 1 year of age

COMPETITIVE ADVANTAGE

- New mechanism of action to improve survival
- Use of small molecules instead of/combined with conventional chemotherapy
- Potential to predict patients' survival depending on HDAC7 levels (co-development of diagnostic kit)

THE SOLUTION

- HDAC7 identified as a prognosis biomarker for t(4;11) pro-B-ALL infants
- Precise and combinatorial therapy for HDAC7 expression induction
- Two small molecule compounds: already tested in combination *in vitro*
- HDAC7 expression impairs t(4;11) pro-B-ALL cells' proliferation
- Promising results in the *in vivo* validation

ADDITIONAL INFO

- PCT patent filed (PCT/EP2022/087132)
- Prestigious grants (DJCLS grant, Fight Kids Cancer, FIS, Gínjol-CERCA Agaur)
- Institut de Recerca contra la Leucèmia Josep Carreras
- Related publications: LINK
- Contact: innovation@carrerasresearch.org

Josep Carreras LEUKAEMIA Research Institute

Figure 1. HDAC7 expression represents a clinical prognostic factor in t(4;11) pro-B-ALL.
Figure 2. Preclinical efficiency, *in vitro* model.

Figure 1

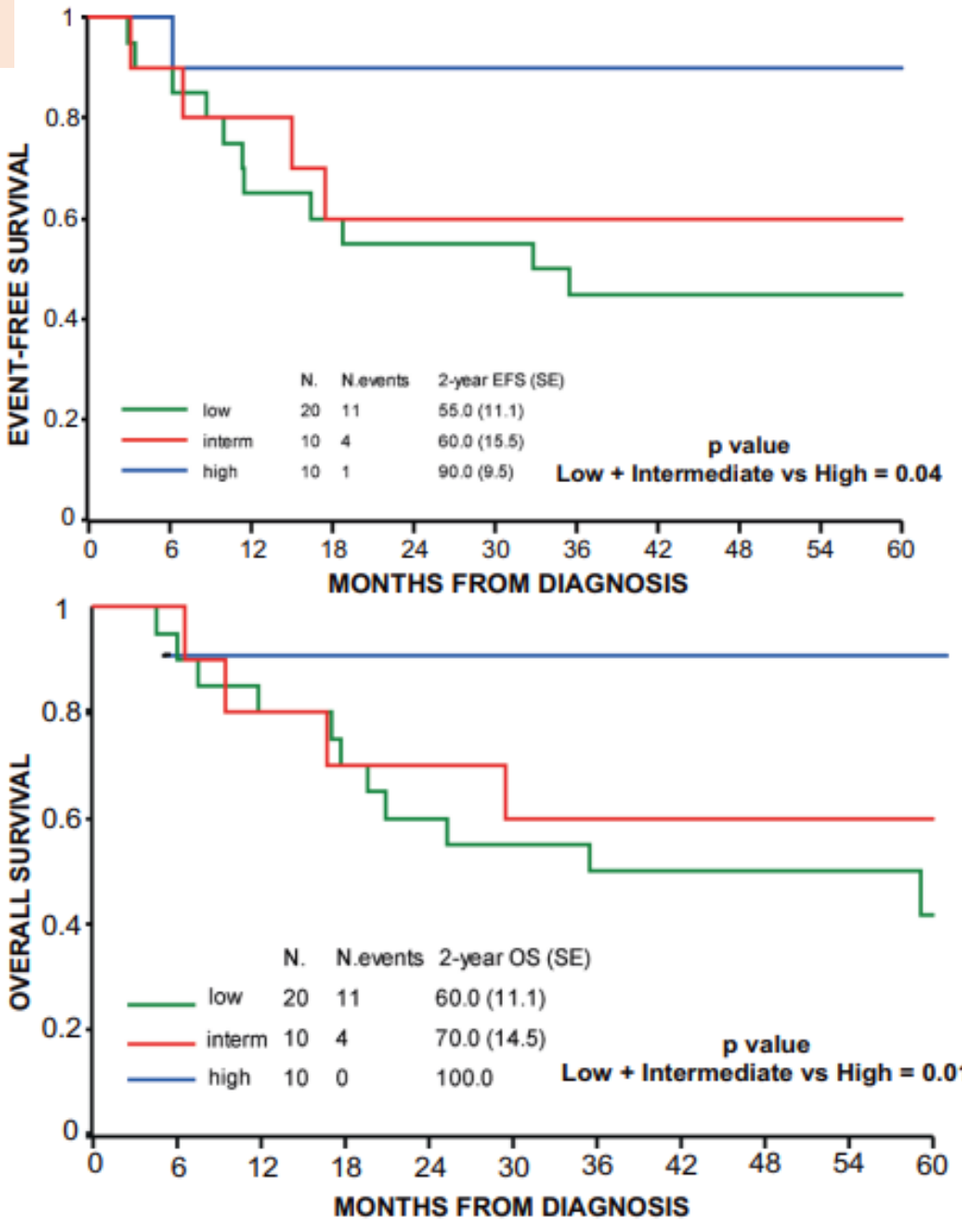

Figure 1. HDAC7 expression represents a clinical prognostic factor in proB ALL. For the Kaplan–Meier EFS (upper panel) and OS (lower panel) plots, the outcome of 40 patients pro-B-ALL patients was analyzed. Patients were assigned to one of the three groups according to the level of HDAC7 expression: HDAC7 high (blue line), HDAC7 intermediate (red line), and HDAC7 low (green line). The numbers of patients allocated to each group is indicated.

Figure 2

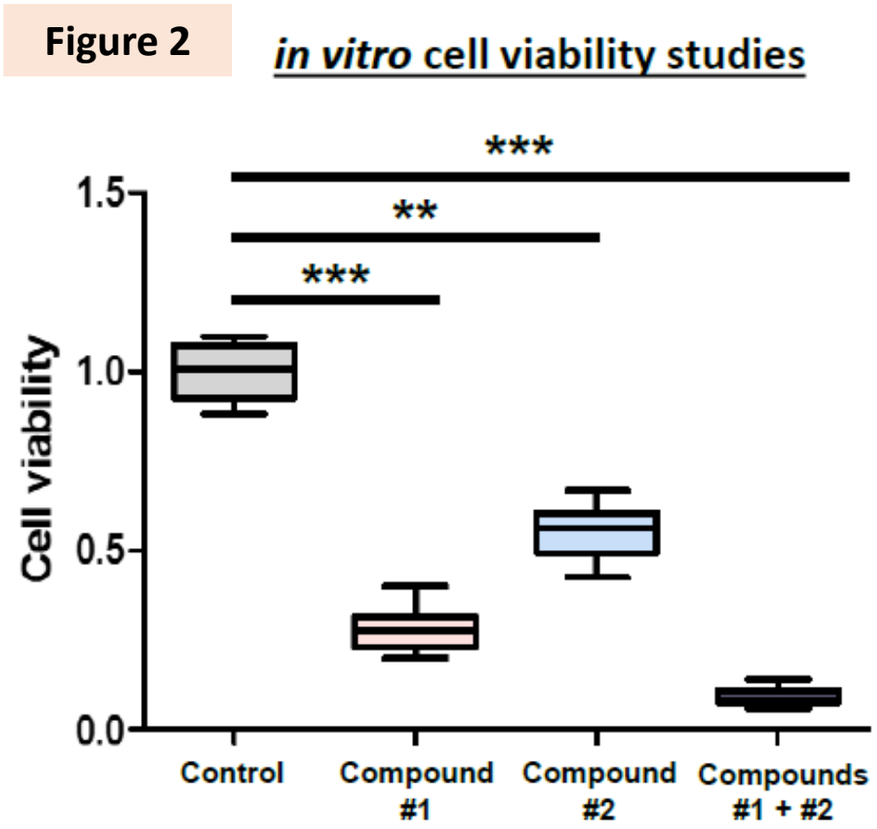

Figure 2. Precise combinatorial therapy with HDAC7-induction capacity reduces t(4;11) pro-B-ALL cells viability. MTT assay to assess cell viability in SEM-K2 pro-B-ALL cells treated with Compound #1 (1 µM, 6 days) and/or Compound #2 (1 µM, 48 hours), or DMSO as control. Statistical significance is indicated as: * $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; or n.s., non-significant.