Intergroup ALFA/GOELAMS Randomized Phase II Trial of Lirilumab as Maintenance Treatment in Elderly Patients with Acute Myeloid Leukemia (EffiKIR Trial)

N. Vey1, H. Dombret2, N. Ifrah3, A. Pigneux4, C. Gardin5, M. Buyse6, P. Andre7, A. Tirouvanziam-Martin7, R. Zerbib7, R. Buffet7, and M. Rozencweig7

1- Institut Paoli-Calmettes, Marseilles, France; 2 - Hopital Saint Louis, Paris, France; 3- CHU Angers, France; 4- CHU Bordeaux, France; 5- Hopital Avicenne, Bobigny, France; 6- IDDI, Brussels, Belgium; 7- Innate Pharma, Marseille, France.

Abstract #TPS3117

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Background

• Placebo controlled, double-blinded, 1:1:1, randomized, 3 arms
• Median LFS does not exceed 15 months after CR1 transplant: Importance of
• Elderly AML patients in CR1 not eligible for HST
• Designed with ALFA and GOELAMS collaborative groups
• Sponsored by Innate-Pharma, Marseille

Endpoints

• Primary Endpoint: Leukemia-Free Survival
• Calculated from the day of randomization until the occurrence of a relapse or death from any cause
• Date of the relapse validated by an Independent Review Committee
• Control LFS estimated at 12 months (placebo group) as determined from ALFA /GOELAMS data base
• Secondary endpoints:
  • Safety (CTCAE v 4.03); safety review by Data and Safety Monitoring Board
  • Time To Relapse, Overall Survival, Leukemia-Specific Survival
  • Exploratory analyses:
    • Pharmacodynamic, KIR occupancy and immunogenicity

Minimization Procedure

• Computerized stochastic minimization according to 4 factors
  • Center
  • Primary versus secondary AML
  • Number of consolidation cycles [1 versus 2]
  • Cyclophosphamides (high versus intermediate risk)
    • As defined according to European Leukemia Net (5)

Survival in Phase I Trial of Maintenance Treatment (IPH2101) in Elderly Patients in Complete Remission From AML

• The 6 patients treated at dose level 1 and 2 mg/kg of the IgG4 paranormal-graded version of anti-KIR showed a significantly improved OS compared to the 16 patients treated at dose level 1 (0.3 mg/kg). 27 months compared to 12.6 months, respectively (p = 0.034 by log-rank test); (2_pages : chemotherapy, growth factors, systemic corticosteroids;

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Timeline

• Recruitement status: Recruiting
• Recruitment period: 15-18 months
• Study start date: October 2012
• Estimated completion date: June 2016

Design

• Placebo controlled, double-blind, 1:1:1, randomized, 3 arms
• Elderly AML patients in CR1 not eligible for HST
• 150 patients to be treated for 24 months
• Monthly administrations during the whole treatment period
• Quarterly clinical follow-up and monthly hematology monitoring after completion of the treatment (Weeks 24, 48, 72 months)
• Designed with ALFA and GOELAMS collaborative groups
• Principal Investigator: Norbert Vey, Paoli-Calmettes Institute, Marseille
• Sponsored by Innate-Pharma, Marseille

Statistical Considerations

• Primary versus secondary AML
• Number of consolidation cycles [1 versus 2]
• Cyclophosphamides (high versus intermediate risk)

Participant:

42 centers in France

References


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• Anti-KIR blockade by IPH2101 (a first generation of anti-KIR antibody) resulted in long-term survival in SCID mice inoculated with lethal autologous AML cells
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Main Inclusion Criteria

• Primary or secondary AML
• First Complete Response (CR) / Complete Response with Downstaging/Partial Response (CR/CR-D) following induction chemotherapy
• Induction chemotherapy performed within the previous 6 months
• Consolidation by 1 or 2 cycles of chemotherapy initiated within 3 months following the induction
• Not eligible for an allogeneic HCT
• Age: > 60 to 80 years
• ECOG: 0-1
• Recovery from acute toxicity of previous antitumor therapy
• Laboratory values at screening:
  • Platelets > 75 x 109 /l, Neutrophils > 1 x 109 /l, Hb > 10 g/dl
  • Adequate renal and liver function

Main Exclusion Criteria

• Good risk cytogenetics including
  • Acute Promyelocytic Leukemia with t(15; 17) or its molecular equivalents
  • Severe auto-immune disease, current active or chronic viral infection, solid organ transplantation
  • Auto-immune or allogeneic hematopoietic cell transplantation, solid organ transplantation
  • Auto-immune disease, current active or chronic viral infection, solid organ transplantation

• 28 days: chemotherapy, growth factors, systemic corticosteroids;

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