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POSTER ABSTRACTS

615.ACUTE MYELOID LEUKEMIAS: COMMERCIALLY AVAILABLE THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

Combination Chemotherapy in Patients with Newly Diagnosed Blastic Plasmacytoid Dendritic Cell Neoplasms (BPDCN): First Results of a Prospective French Trial (LpDessai)

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Introduction

Blastic plasmacytoid dendritic cell neoplasms (BPDCN) are now well-characterized diseases clearly referenced in the 5 th edition of the World Health Organization (WHO) Classification of Tumors (2022) [1] but treatment remains a real challenge. There is no consensus on the first line treatment even if CD123 targeted therapies are available in the USA and some European countries. Standard chemotherapy remains largely used as first line treatment with better results of leukemia-based regimens despite a high toxicity rate in this frail population [2,3]. To establish a reference chemotherapy scheme, we prospectively evaluated the efficacy and toxicity of a combination chemotherapy (idarubicin, methotrexate, L-asparaginase, and dexamethasone) in newly diagnosed BPDCN patients (pts) in France.

Patients and methods

This single stage phase II study enrolled consecutive adult pts with suspected BPDCN in participating French centers. BPDCN diagnosis was centrally reviewed for cytology and immunophenotype (IF) (Pr Garnache Ottou F, UMR RIGHT BESANCON) and if needed for histology (Dr Petrella T, Montréal, Canada) according to published recommendations [1,4]. After giving their informed consent, patients were evaluated for tumoral involvement by PET-scan, systematic lumbar puncture, and the mSWAT score was calculated for skin extension. Patients then received three 21 days-cycles of Ida/Metho/L-asp/Dex combination, before evaluation. Eligible patients with complete response (CR), complete response with incomplete bone marrow recovery (CRi) or partial response (PR) underwent allogeneic hematopoietic stem cell transplantation (HCT). Those not eligible received consolidation chemotherapy with 28 days cycles of Metho/L-asp/Dex (Figure 1). The primary objective was the proportion of patients with CR after 3 cycles of chemotherapy. Secondary objectives were the proportion of patients with an objective response (ORR) defined as CR, CRi or PR, the minimal residual disease (MRD) in responding patients evaluated by the presence of plasmacytoid dendritic cell blast measured by flow cytometry in the bone marrow, the incidence of severe adverse events and overall survival (OS).

The competent ethics committee (Comité de Protection des Personnes Île de France 8) approved the study. The Besançon University hospital promoted the trial, financed by a grant of the French National Cancer Institute (INCa-DGOS_11093).

Results

Twenty-eight pts, originating from 16 centers, were screened between May 2019 and March 2023. Two patients with a misdiagnosis were screen failures. Two patients did not receive the planned chemotherapy due to clinical deterioration; 24 patients (21 male, 3 female) received at least one chemotherapy cycle and 23 are analyzed with a current end-point on June 30, 2023. Median age was 65y (21-79y). ECOG status was 0-1 in 20 cases, and 2 in 3 cases. A cutaneous involvement was identified in 16 pts (70%) and an extra medullary involvement was present in 13 (62%) pts: spleen, n= 6 (25%); lymph nodes, n= 7 (30%). Twenty-three pts (90%) had a bone marrow infiltration (identified only on IF in 4 cases), and 3 cases (14%) a documented central nervous system involvement.

Nine pts had to stop planned treatment due to severe adverse events (3 deaths, 4 acute renal failure and 2 grade 4 febrile neutropenia) and in 4 pts, at least one cycle had to be delayed.

Among the 15 pts receiving at least 3 cycles, 12 (80% and 50% of the whole cohort) were in ORR (CR = 8, CRi = 2, PR = 2) after the 3rd cycle of chemotherapy, 2 pts did not respond. Eight of ten (80%) CR/CRi pts had a MRD $< 10^{-4}$ without any further relapse. Nine of 12 responding patients (75%) received an allogeneic HCT 1-2 months after the end of the 3 rd cycle. Global OS at 6 months for responding or failing pts were 100% and 37% respectively (Figure 2).

Conclusion

In selected pts, an adapted chemotherapy could offer high CR rate in pts able to follow the planned treatment but remains toxic in frail pts, with only half of the them achieving a 3 rd cycle of chemotherapy. We confirm that pts achieving ORR and receiving HCT obtain prolonged CR. MRD level seems to correlate with OS and could be a useful tool to manage treatment toxicity in BPDCN frail pts.

References:

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Figure 1 : Schedule of the LpDESSAI Protocol
Asp = asparaginase; CR = complete remission; CRi = complete remission with incomplete hematopoietic recovery; D = Day; Dex = dexamethasone; HCT = allogeneic stem cell transplantation; Ida = idaruricin; M = month; MTX = methotrexate

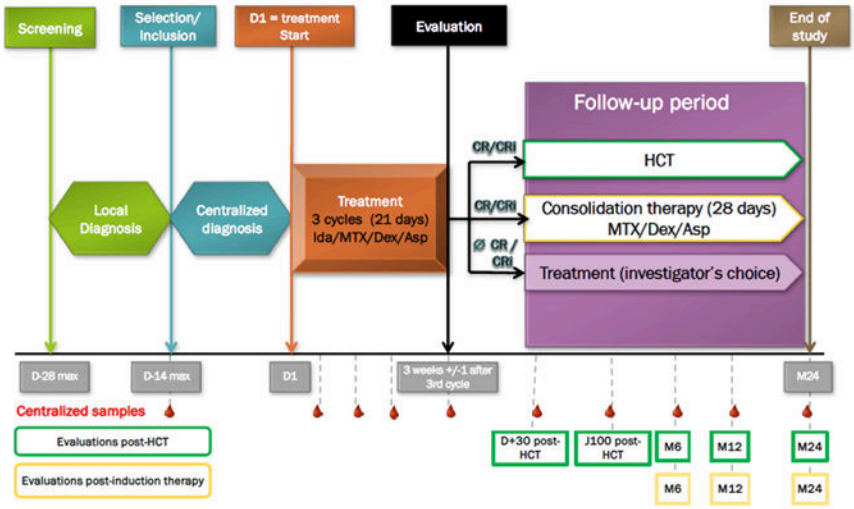

Figure 2 : Overall survival according to the response to initial chemotherapy
SUCCESS (ORR at 3 cycles) - - - - -
FAILURE (disease progression or treatment stopped after severe adverse event before the 3rd cycle) ——

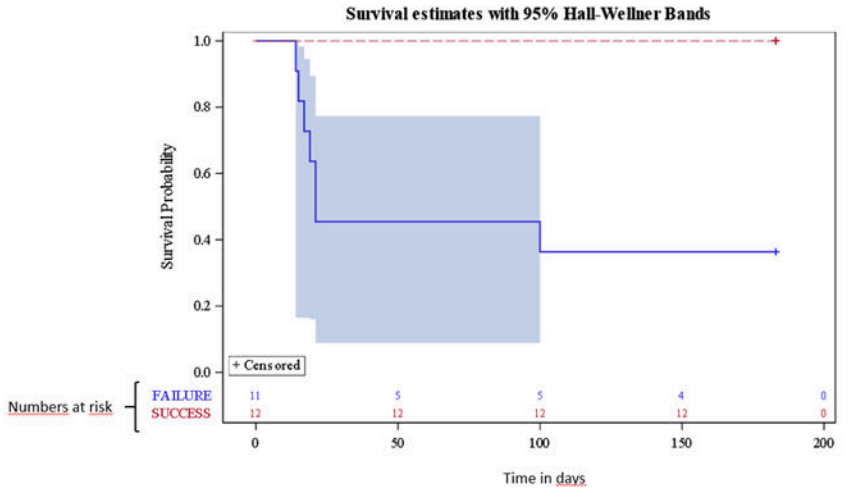

Figure 1

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