

Combination Chemotherapy with Nipent®, Cytoxan®, and Rituxan® (PCR) Induces High Rate of Remissions

Including Complete Responses and Achievement of Minimal Residual Disease in Previously Untreated B-Chronic Lymphocytic Leukemia

Abstract # 339
Lead Author: Neil Kay

In an oral session, researchers from Mayo Clinic and Ohio State University presented an interim analysis of Nipent®, (pentostatin) Cytoxan®, (cyclophosphamide) and Rituxan® (rituximab) in 33 patients with progressive previously untreated CLL. Nipent® (2 mg/m²), Cytoxan® (600 mg/m²) and Rituxan® (375 mg/m²; omitted on week one) were all administered on day one, every three weeks, for a maximum of six cycles. Patients received prophylactic trimethoprim-sulfamethoxazole (TMP/SMX) and Zovirax® (acyclovir), and granulocyte-colony stimulating factor (G-CSF) support. Seventeen of 33 patients had high Rai stage, 25 were male, the median age was 62 years, 20 had one detectable chromosomal abnormality by fluorescent *in situ* hybridization (FISH) and eight had ≥ two anomalies.

Partial response (PR) or better was achieved in 97% (32/33). Bone marrow reviews two months post-treatment showed 13 complete remissions (CRs), 11 nodal partial responses (nPRs) and nine PRs.* No differences were found between type of response and mutation status

Combination Rituximab, Pentostatin, and Cyclophosphamide as Frontline CLL Therapy

- Single-arm, phase 2 trial
- 33 patients with progressive untreated CLL received
 - Rituximab (375 mg/m²) Day 1
 - Not given during first week
 - Pentostatin (2 mg/m²) Day 1
 - Cyclophosphamide (600 mg/m²) Day 1
 - Every 3 wks for max 6 cycles
- Patients also received
 - G-CSF support
 - TMP/SMX prophylaxis
 - Acyclovir prophylaxis
- 97 of patients responded
 - Complete response, 13 (39%)
 - Nodal partial response, 11 (33%)
 - Partial response, 9 (28%)
- Most common Gr 3/4 events
 - Neutropenia, 19 (57%)
 - 33% Gr 4
 - Thrombocytopenia, 6 (18%)
 - Nausea/vomiting, 5 (15%)

Kay NE, et al. ASH 2004. Abstract 339.
<http://clinicaloptions.com/onco>

(17 non-mutated immunoglobulin heavy chain variable region [IgVH]) or CD38⁺ status (67% negative). Of 27 patients with post-treatment FISH analyses, 25 became normal after treatment. Of the remaining two patients, one improved from 94% to 27.5% abnormal nuclei after treatment, the other patient died on study. Minimal residual disease (MRD) was established by three-color flow cytometry to detect CD5⁺/CD19⁺/CD79b⁻ B cells. All patients had a reduction in B cells (median reduction 91%) with more variable reduction noted in the nPR group. Grade ≥ 3 toxicities were observed in 22 patients, with neutropenia

being the most common event (n=19). No patient required red blood cell (RBC) or platelet transfusions and no severe infections were observed.* The most common non-hematological toxicity observed was nausea/vomiting (n=5).* One patient died of hypoxia and hypotension, possibly related to treatment. First-line treatment with the novel regimen polymerase chain reaction (PCR) demonstrated significant clinical activity irrespective of risk stratification parameters with rapid response induction and modest toxicity.

*Data updated from abstract to reflect data presented at podium presentation.

Abnormality	13q-	+12	11q-	17p-	t(14;18)	6q-	MDM2
Number of patients	17	8	7	2	1	1	1

33 patients total: five pts = no detectable chromosomal abnormalities by FISH at baseline, 20 pts = one FISH anomaly, eight pts = two or more FISH anomalies. Of all 28 patients with any anomaly, the above specific abnormalities were detected.

Nipent® and Cytoxan with or without Rituxan® Has Significant Activity

In Patients with Previously Treated Chronic Lymphocytic Leukemia and Other Low Grade Lymphoid Neoplasms

Abstract # 3484
Lead Author: Nicole LaManna

Researchers from Memorial Sloan-Kettering Cancer Center and Cleveland Clinic Foundation presented their cumulative experience with Nipent® and Cytoxan® (PC, n = 23), and Nipent®, Cytoxan®, and Rituxan®, (PCR, n=46) in previously treated CLL patients. Nipent® (4 mg/m²), Cytoxan® (600 mg/m²) ± Rituxan® (375 mg/m²; omitted on week one) were all administered on day one, every three weeks for a maximum of six cycles. Patients received hydration,

prophylactic trimethoprim-sulfamethoxazole (TMP/SMX), Zovirax®, granulocyte-colony stimulating factor (G-CSF) and antiemetics. The median age 64 (PC) and 62 (PCR group) and the median number of pre-treatments was three (PC) and two (PCR). Responses were observed in 74% (17% CR of the PC group and 79% (29% CR) of the PCR group. A 50% PR was observed in 10 of 14 evaluable patients with other low-grade B cell diseases (eight small lymphocytic

lymphoma [SLL], two Waldenstrom's macroglobulinemia [WM], four follicular lymphoma). Previously presented data demonstrate a 77% response in fludarabine-refractory patients (*J Clin Oncol.* 2003 Apr 1;21(7):1278-84). The regimens were well tolerated with grade 3-4 toxicities consisting primarily of myelosuppression and its complications. PC and PCR are highly active and well tolerated in heavily pretreated patients.