Session 11: T-cell lymphomas

125 DURABLE REMISSIONS WITH SGN-35 (BRENTUXIMAB VEDOTIN): UPDATED RESULTS OF A PHASE 2 STUDY IN PATIENTS WITH RELAPSED OR REFRACTORY SYSTEMIC ANAPLASTIC LARGE CELL LYMPHOMA (SALCL)

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Introduction: sALCL is a CD30-expressing malignancy comprising ~2-3% of NHL cases. SGN-35 comprises an anti-CD30 antibody conjugated by a plasma-stable linker to the potent antimicrotubule agent, monomethyl auristatin E (MMAE). SGN-35 selectively induces apoptotic death of CD30+ cells by binding, internalizing, and releasing MMAE.

Methods: A phase 2, single-arm, multicenter study evaluated the efficacy and safety of SGN-35 in patients (pts) with relapsed or refractory sALCL. Pts received SGN-35, 1.8 mg/kg q3 wks as a 30-min. outpatient IV infusion for up to 16 cycles. The primary endpoint was the objective response rate (ORR) per an independent review facility (IRF) according to Cheson 2007.

Results: 58 pts were enrolled; 57% male, median age = 52 yrs (14C76). 72% of pts were ALK negative. Pts had received a median of 2 (1C6) prior systemic therapies. 62% of pts had primary refractory disease, 50% were refractory to their most recent prior therapy, and 22% had never responded to any prior therapy. At the time of primary efficacy analysis, ORR per IRF was 86% (50 of 58 pts) with CRs in 53% of pts (31 of 58). Median duration of objective response had not yet been reached; duration ranged from 0.3 to 45.3 wks. Of 15 pts with malignant cutaneous lesions at baseline, 14 (93%) had resolution of all lesions; median time to resolution was 4.9 wks. After achieving a remission with SGN-35, 7 pts received an allogeneic stem cell transplant (SCT) and 7 pts had an autologous SCT. Treatment-related AEs in ≥ 15% of pts were peripheral sensory neuropathy (36%), nausea (24%), fatigue (22%), diarrhea (19%), and neutropenia (17%). AEs ≥ Grade 3 in ≥10% of patients were neutropenia (21%), thrombocytopenia (14%), and peripheral sensory neuropathy (10%). No treatment-related Grade 5 events were observed.

Conclusions: SGN-35 induced objective responses in 86% of pts with highly refractory sALCL, including a high proportion of CRs, with manageable AEs. Updated response durability and safety will be presented.

126 PRELIMINARY RESULTS FROM AN OPEN-LABEL, MULTICENTER, PHASE II STUDY OF BENDAMUSTINE IN RELAPSED OR REFRACTORY T-CELL LYMPHOMA FROM THE FRENCH GOELAMS GROUP: THE BENTLY TRIAL

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Background: Bendamustine is a cytotoxic agent showing structural similarities but no cross-resistance with alkylating agents or antimetabolites. It has been recently approved for the treatment of CLL and follicular lymphoma. Preliminary data showed that this compound is active against T-cell lines. The aim of this phase 2, single-arm, open-label study was to evaluate the activity ofBen in patients (pts) with progressive or relapsed T-cell lymphoma.

Patients and Methods: Pts with histologically confirmed T-cell lymphoma (PTCL nos, AILD, ALCL, other subtypes) or Mycosis Fungoide (MF) ≥ stage IIB who failed or were refractory to ≥ 1 prior systemic therapy, and had measurable disease and ECOG performance status ≤3 were eligible. Pts received Bendamustine at the dosage of 120 mg/m^2 as a 1-h IV infusion on days 1-2, every 21 days for 3 cycles; Pts with complete (CR), partial remission (PR) or stable disease (SD) were then eligible for additional 3 cycles. The primary endpoint was the overall response rate ORR (CR + CRu + PR) using International Working Criteria for non-Hodgkin's lymphoma.

Results: The first 38 evaluable pts who received at least 1 cycle of Bendamustine were analyzed. All of them had histologically confirmed PTCLu (n=13); AILD (n=22); EATL (n=1); MF (n=2). There were 28 male and 10 female with a median age at diagnosis of lymphoma of 64 years (38-87). Median time from diagnosis to enrolment was 11 mo (5-111). 34 pts presented with Ann Arbor stage III-IV and 2 pts with stage II. 2 pts had MF stage IIB. Median number of prior systemic therapies was 2 (range, 1-3). 5 pts (16%) had failed to prior SCT. The best response to previous therapy was CR+CRu (n=13), PR (n=10), SD (n=3), progressive disease (PD, n=10) and 2 pts were not evaluable. At final evaluation (after 6 cycles or premature end of treatment) of Ben, the ORR was 47% including CR+CRu in 11 pts (29%) and PR in 7 pts (18%). 20 pts experienced progressive disease (53%). At the time of analysis, the median duration time for responder pts was 157 days (14-350). The most frequent adverse events (AEs≥G 3-4) were neutropenia (28 episodes), thrombopenie (18 episodes). Grade 1-4 infections were recorded in 24 episodes. G3-4 cutaneous, pulmonary and cardiac toxicity were noted in 5, 3 and 2 episodes respectively. SAEs were reported in 23 patients (35 episodes). Sepsis was the most frequent cause of SAEs.

In conclusion, complete and durable responses were observed with Bendamustine used as a single agent in pts with relapsed or refractory PTCL.These data support the therapeutic potential for Ben in PTCL and suggest that this drug is a promising candidate for inclusion in future novel regimens for these diseases.

127 LONG-TERM OUTCOME OF ADULTS WITH SYSTEMIC ANAPLASTIC LARGE-CELL LYMPHOMA TREATED WITHIN THE GROUPE D'ETUDE DES LYMPHOMES DE L'ADULTE (GELA) TRIALS

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Introduction: The long-term outcome of adults with systemic anaplastic large-cell lymphoma (ALCL) is not known. Moreover the independent prognostic value of ALK expression remains debated.

Patients and Methods: Eligibility criteria included adults with confirmed diagnosis of systemic ALCL after immunohistopathological review and defined ALK expression status. Patients were retrieved from the GELA LNH87-LNH93-LNH98 prospective clinical trials.

Results: Of the 138 included patients with systemic ALCL, 64 (46%) were ALK+ and 74 (54%) were ALK-. They were treated between october 1987 and march 2003, and the stopping date was 1st January 2009. The median follow-up duration was 8 years. At diagnosis, patients with ALK+ ALCL were younger than those with ALK- ALCL (median age 31.5 vs 56 years, p<.0001) with significantly more patients < 40 years in ALK+ group (66% vs 23%, p<.0001). The performance status (PS) was poor (more than 1) in 16% (ALK+) vs 33% (ALK-) (p=.020). Most patients had advanced-stage disease (ALK+, 56%; ALK-, 67%). The IPI score was high (3-5) in 23% (ALK+) vs 48% (ALK-) (p=.030). β2 microglobulin (level available in 90/138 patients) was > 3 mg/L in 12% (ALK+) vs 33% (ALK-) (p=.017). Number of extranodal sites > 1, bulky disease (mass > 10 cm), and elevated LDH had a similar distribution in ALK+ and ALK- patients. All but one patients received an anthracyclin-based regimen. Twenty two patients (ALK+, n=16; ALK-, n=6) underwent planned upfront high-dose therapy and autologous stem-cell transplantation (HDT-ASCT). The overall response rate to first-line treatment was better in ALK+ than in ALK- patients (89% vs 76%, p=.042). After 3 years, there was no relapse in ALK+ group, whereas 3/26 relapses in ALK- group (2 relapses after 5 years). The 8-year overall survival (OS) was 82% in ALK+ vs 49% in ALK- (p<.0001). Prognostic factors for OS identified by multivariate analysis were β2 microglobulin (p=.0004) and age (p=.029) in the whole cohort; number of extranodal sites > 1 (p=.02) in ALK+ ALCL; β2 microglobulin (p=.01), liver involvement (p=.004), albumin (p=.01) and IPI (p=.0007) in ALK- ALCL. OS at 8-year was

significantly better in transplanted patients than in matched controls (77% vs 47%, p=.03).

Conclusion: This long-term study allowed us to refine the prognosis of adults with systemic ALCL and suggested a potential benefit of upfront HDT-ASCT in selected cases.

128 CHOEP-14 AND AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT) IN ANGIOIMMUNOBLASTIC T-CELL LYMPHOMA: PROSPECTIVE STUDY BY THE NORDIC LYMPHOMA GROUP (NLG-T-01)

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Angioimmunoblastic T-cell lymphoma (AIL) accounts for 15–20% of primary systemic T-cell lymphomas (PTCL) which usually have a poor prognosis. AIL is associated with EBV, presents often as advanced disease, accompanied by low performance status (PS), B symptoms and high LD. Median survival is < 3 years when treated with conventional chemotherapy.

The NLG-T-01 trial included 160 patients, age 18-67 yrs with systemic alk-negative PTCL in the Nordic countries during 2002 - 2007. Treatment consisted of CHOEP-14 x 6 followed by ASCT after BEAM or BEAC in responsive patients. Patients > 60 yrs received CHOP-14 as induction. A total of 30 AIL patients were enrolled (19% of all included). Median age was 57 yrs, range 39–67. PS was ≥ 2 in 8 patients (27%). 24 patients (80%) had stage III-IV, 22 (73%) had elevated LD, 20 (67%) had B symptoms and 3 (10%) had bulky disease.

Response status after 3 and 6 courses were CR/CRu in 50% and 63% of the patients, respectively.

20 of 30 AIL patients (67%) received BEAM / BEAC and ASCT. Overall response rate after 6 courses was 87% and for those who underwent ASCT 80%, indicating that some patients had rapid progressive disease after induction therapy or shortly after ASCT.

13 patients died, 10 of lymphoma, 2 due to toxicity, 1 of septicaemia. In the present analysis, median follow up time is 32 months for the 17 AIL patients alive. The 4 yr progression free and overall survival are 47% and 50%, respectively.

CHOEP-14 plus ASCT is effective and feasible as first line treatment of AIL, although early relapses remain a problem. The role of EBV and the addition of biological agents are being studied.

129 ENTEROPATHY-ASSOCIATED T-CELL LYMPHOMA: CLINICAL AND HISTOLOGICAL FINDINGS FROM THE INTERNATIONAL PERIPHERAL T-CELL LYMPHOMA PROJECT

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Introduction: Few large international series of enteropathy-associated T-cell lymphoma (EATL) have been reported.

Materials and Methods: We studied a cohort of 62 patients with EATL among 1153 patients with peripheral T- or NK-cell lymphoma from 22 centers worldwide. The diagnosis was made by a consensus panel of four expert hematopathologists using the WHO criteria. Clinical correlations and survival analyses were performed.

Results: EATL comprised 5.4% of all lymphomas in the study and was most common in Europe (9.1%), followed by North America (5.8%) and Asia (1.9%). As expected, the small intestine was the most commonly involved site at diagnosis (90%), followed by the large intestine (16%), with frequent involvement of mesenteric (35%) and para-aortic or iliac lymph nodes (11%). EATL type 1 (66%) was more common than type 2 (34%), and was especially frequent in Europe (79%). A clinical history of celiac sprue was present in 32.2% of the patients and was associated with both EATL type 1 and type 2. A tumor of ≥ 5 cm at diagnosis was reported predominantly in patients with EATL type 2 (p = 0.02). There were no other distinguishing clinical features between EATL type 1 and type 2. The median overall survival in EATL was only ten months and the median failure-free survival was only six months. A clinical history of celiac sprue, a large tumor mass (≥ 5 cm) at diagnosis, an elevated serum LDH level and increased C-reactive protein (CRP) were adverse predictors of survival. EATL subtype or other biological parameters did not accurately predict survival. The International Prognostic Index (IPI) was not a good predictor of survival in contrast with the Prognostic Index for Peripheral T-cell lymphoma (PIT). A history of clinical sprue was the only clinical variable that predicted for adverse survival independently of the PIT.

Conclusion: Our study confirms the poor prognosis of patients with EATL and the need for improved treatment. Our study also shows that a history of clinical sprue as well as the PIT may be used to predict survival. In addition, EATL type 1 and type 2 do not show major clinical differences, except for larger tumor masses in EATL type 2.