LymphomaHub

ASH 2018

Practice changing abstracts in non-Hodgkin lymphoma (NHL) and chronic lymphocytic leukemia (CLL)

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Treatment developments in CLL

#LBA-4: A randomized phase III study of ibrutinib (PCI-32765)-based therapy vs. standard fludarabine, cyclophosphamide, and rituximab (FCR) chemoimmunotherapy in untreated younger patients with chronic lymphocytic leukemia (CLL): a trial of the ECOG-ACRIN cancer research group (E1912)

https://lymphomahub.com/medical-information/ash-2018-ibrutinib-plus-rituximab-provide-superior-outcomes-than-fcr-in-naive-cll-patients-results-from-the-ecog-acrin-phase-iii-trial-e1912

#LBA-7: Acquisition of the recurrent Gly101Val mutation in BCL2 confers resistance to venetoclax in patients with progressive chronic lymphocytic leukemia

https://lymphomahub.com/medical-information/novel-bcl2-mutation-leads-to-venetoclax-resistance-in-progressive-cll-patients

#691: Ibrutinib + obinutuzumab versus chlorambucil + obinutuzumab as first-line treatment in patients with chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL): results from phase 3 iLLUMINATE

https://lymphomahub.com/medical-information/ash-2018-results-from-the-phase-iii-illuminate-trial-on-chemotherapy-free-first-line-treatment-for-cll-sll

Comments provided by Francesc Bosch

- **#LBA-4:** Superiority of ibrutinib + rituximab over the standard FCR. Although not powered enough for subgroup analysis, ibrutinib was clearly superior to FCR in unmutated IGHV, and at least equivalent in mutated IGHV. Therefore, ibrutinib is confirmed as the best front line treatment in CLL
- **#LBA-7:** First description of mutations in BCL2 gene in patients receiving venetoclax. Although the molecular mechanisms are not completely unveiled, these results reinforce the concept of limited duration of these novel therapies for the purpose of avoiding resistance
- **#691:** Randomized trial comparing ibrutinib + obinutuzumab *vs* chlorambucil + obinutuzumab in frail patients. The former combination proved to be superior in both PFS and deepness of response. The caveat of this study is the addition of obinutuzumab to chlorambucil, probably a strategy that will not be implemented in clinical practice, since it does not imply the cessation of the treatment

Improving the standard-of-care in aggressive NHL (I)

#781: Excellent outcome of young patients (18-60 years) with favorable-prognosis diffuse large B-Cell lymphoma (DLBCL) treated with 4 cycles CHOP plus 6 applications of rituximab: results of the 592 patients of the Flyer trial of the Dshnhl/GLA

https://lymphomahub.com/medical-information/ash-2018-results-from-the-flyer-trial-on-the-efficacy-of-four-r-chop-cycles-versus-six-in-young-nhl-patients

#783: No added benefit of eight *versus* six cycles of CHOP when combined with rituximab in previously untreated diffuse large B-Cell lymphoma patients: results from the international phase III GOYA study

https://lymphomahub.com/medical-information/ash-2018-results-from-the-phase-iii-goya-trial-r-chop-versus-g-chop-for-first-line-dlbcl

Comments provided by Anton Hagenbeek

- **#783:** In this sub-analysis of the GOYA trial, results in patients treated with 6 x R-CHOP (n = 526) and 8 x R-CHOP (n = 186) given 3-weekly were compared. These were patients with IPI ≥ 2. The number of courses was at the discretion of each participating center. No difference in 3-year PFS and OS were noted, but more toxicity was reported, i.e. grade III-IV AEs, including all grade infections (17.8% *vs* 38.9%, respectively) and SAEs in 12.2% *vs* 20.1% of patients. No conditions could be identified where patients had benefit from 8 courses, such as initial bulky disease, high IPI, ABC subtype, or PR at interim PET. The authors stated that 6 x R-CHOP is the treatment of choice in this patient category with IPI ≥ 2

Comments provided by Anton Hagenbeek

- **#781:** Good news for younger patients (18–60 years) with favorable prognosis DLBCL (aaIPI = 0): 4 courses of R-CHOP plus 2 additional infusions of rituximab yielded identical results if compared with the conventional regimen of 6 courses of R-CHOP in the prospective randomized FLYER trial in 592 patients. Thus, 33% less CHOP exposure, non-inferior efficacy and less toxicity. CR rates did not differ between both arms (91% *vs* 92%, respectively), with a median follow-up of 66 months. PFS at 36 months was 96% *vs* 94%, and OS 99% *vs* 98%, respectively. Excellent results which makes this shortened treatment strategy standard-of-care in this particular patient population

Improving the standard-of-care in aggressive NHL (II)

#997: The ECHELON-2 trial: results of a randomized, double-blind, active-controlled phase 3 study of brentuximab vedotin and CHP (A+CHP) versus CHOP in the frontline treatment of patients with CD30+ peripheral T-cell lymphomas

https://lymphomahub.com/medical-information/brentuximab-vedotin-plus-chemotherapy-for-cd30-ptcl-results-from-the-phase-iii-echelon-2-trial

Comments provided by Anton Hagenbeek

- **#997:** For the first time in the history of T-cell lymphoma a study showing an increase in OS is reported, in this case by adding the anti-CD30 drug-conjugate brentuximab vedotin (Adcetris®) to CHP (CHOP without Vincristine; n = 226) and comparing this to CHOP (n = 226). Patients with CD30+ peripheral T-cell lymphoma were eligible for inclusion. Median PFS was 48.2 months *vs* 20.8 months, respectively (HR = 0.71). Median OS has not been reached in both arms but treatment with Adcetris®-CHP reduced the risk of death by 34% compared with CHOP (HR = 0.66; *P* = 0.0244). The study did not allow the authors to reach strong conclusions in the various subgroups of T-cell lymphoma, such as the most frequently occurring peripheral T-cell lymphoma NOS. Based on the results of this ECHELON-2 study, A-CHP is a major achievement and may be regarded as standard-of-care in peripheral T-cell lymphoma

Indolent NHL

#445: AUGMENT: A phase III randomized study of lenalidomide plus rituximab (R2) vs rituximab/placebo in patients with relapsed/refractory indolent non-Hodgkin lymphoma

https://lymphomahub.com/medical-information/ash-2018-results-from-the-phase-iii-augment-trial-lenalidome-plus-rituximab-for-r-r-fl-and-mzl

https://lymphomahub.com/medical-information/nathan-fowler-ash-2018-long-term-updates-on-lenalidomide-plus-rituximab-in-fl

Comments provided by Gilles Salles

- With the benefits observed in term of response, PFS and overall survival for patients with follicular lymphoma, these results represent an important step moving forward in providing the R2 regimen available to physicians and patients for 2nd (or further) lines of therapy
- Given the RELEVANCE study results (showing efficacy similarity between R2 and R-chemo in 1L patient) it's likely the R2 will become a very popular regimen in patients with FL when approved by health authorities
- The future of this combination for patients with other indolent lymphoma subtypes is much less clear

Comments provided by Stefano Luminari

- Superiority of R2 over rituximab was confirmed not only for the primary endpoint but also for ORR, CR rate, duration of response and, also if the study was not powered for secondary endpoints, in terms of 2-year OS rate for the largest group of FL patients
- New data and update of existing studies with R2 do not show any new and unexpected safety alert and confirm the option as safe and manageable
- The median PFS of 39.4 months is highly encouraging and favorably compares with other immunochemotherapy options in the setting of RR FL
- The R2 chemofree can easily find his place as new standard option for relapsed refractory patients with FL