



Practice-changing abstracts selected by the
Lymphoma Hub Steering Committee

61st ASH Annual Meeting & Exposition

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The **world-leading experts** in lymphoma and CLL shared the top abstracts from ASH 2019 that they believe could have the **greatest impact on clinical practice.**

In this document, you will find comments from the Lymphoma Hub Steering Committee members on DLBCL prognostic factors, MCL novel treatment options, FL chemo-free treatment options, treating patients with newly diagnosed CLL, R/R CLL, and poor-prognosis NHL, and the role of maintenance therapy in Waldenström's macroglobulinemia.

DLBCL: Prognostic factors

#487: The Optimal Timing of Interim 18F-FDG PET in Diffuse Large B-Cell Lymphoma: An Individual Patient Data Meta-Analysis By the Petra Consortium



Professor Judith Trotman

“This large, individual patient data meta-analysis is most informative, confirming the important prognostic value of iPET4 to identify patients for whom alternative therapies need study. Both delta SUV and Deauville score (DS) 5 are useful discriminators and standardization of acquisition and reporting of these parameters will be key to advancing interim-PET adapted approaches in lymphoma.”



Doctor Astrid Pavlovsky

“The benefit of using interim PET-CT in DLBCL is not well defined. This valuable meta analysis shows the prognostic value of a negative iPET2, but suggests that iPET4 is the optimal time to identify non-responders. It is still to evaluate whether change of therapy at this time improves PFS and OS.”

PET in DLBCL | Interim PET as a biomarker for response and PET-directed therapy for limited stage DLBCL

The prognostic value of 18F-FDG-PET metabolic heterogeneity in DLBCL after first-line immunochemotherapy

Educational theme | PET as a prognostic tool in lymphoma

#400: Age and Time to Progression Predict Overall Survival (OS) in Patients with Diffuse Large B-Cell Lymphoma (DLBCL) Who Progress Following Frontline Immunochemotherapy (IC)



Professor Irene Biasoli

“Recently, new treatment approaches, such as chimeric antigen receptor T-cell therapy, emerged as an effective therapy for relapsed or refractory DLBCL patients. In this robust analysis, the authors identified an easy-to-apply prognostic tool for this population setting using age and time to progression after first treatment. It will enable a better selection of cases who might benefit from new cost-intense and complex gene or cell therapies.”



Doctor Astrid Pavlovsky

“This is important information regarding outcome in R/R DLBCL, and its value relies on the great number of patients included in the analysis and in the external validation.”

How can predicting survival in patients with relapsed DLBCL improve treatment decisions?

New prognostic model for survival in patients with R/R DLBCL

DLBCL: Prognostic factors

#349: PET-Directed Therapy for Patients with Limited-Stage Diffuse Large B-Cell Lymphoma - Results of Intergroup Nctn Study S1001



Professor Anton Hagenbeek

“I found abstract #349 most promising because in limited-stage DLBCL, a negative PET scan after the first 3 courses of R-CHOP keeps the patient away from additional radiotherapy, preventing late effects. This finding might be considered as a change in daily practice.”



Doctor Astrid Pavlovsky

“The results of this trial, together with the previously reported FLYER trial, supports that a PET-adapted therapy in limited-stage DLBCL is safe. R-CHOP x 4 can be a new standard of treatment for patients who achieve a negative PET after 3 cycles of R-CHOP. According to these results, this will allow us to de-intensify treatment in more than 90% of patients.”

[Which patients with DLBCL may benefit from PET-directed induction therapy?](#)

[PET in DLBCL | Interim PET as a biomarker for response and PET-directed therapy for limited stage DLBCL](#)

[The prognostic value of PET scan in the treatment of DLBCL](#)

#398: Definition and Validation of the New Elderly Prognostic Index (EPI) for Elderly Patients with Diffuse Large B-Cell Lymphoma Integrating Geriatric and Clinical Assessment: Results of the Prospective “Elderly Project” on 1353 Patients By the Fondazione Italiana Linfomi



Professor Irene Biasoli

“This is relevant clinical information coming from a multicenter, prospective, observational analysis on more than 1,100 elderly patients with DLBCL. The creation of a new prognostic index for the elderly population allowed the identification of 3 risk groups within terms of overall survival. Also, the new tool incorporates simplified geriatric scales with IPI and hemoglobin that could be very useful and easy to apply in clinical practice.”



Doctor Astrid Pavlovsky

“There is no doubt we should integrate a geriatric assessment before deciding treatment in elderly patients with DLBCL. This score integrates a simplified geriatric assessment with clinical features and contributes to treatment decisions in a group of patients with a heterogenous outcome.”

[Why is an elderly prognostic index required for patients with DLBCL?](#)

[How should we use geriatric assessment to guide treatment decisions for elderly patients with DLBCL?](#)

#490: Molecular Characteristics and Disease Burden Metrics Determined By Next-Generation Sequencing on Circulating Tumor DNA Correlate with Progression Free Survival in Previously Untreated Diffuse Large B-Cell Lymphoma



Professor Ulrich Jager

“I found this abstract very intriguing because it showed the importance of molecular subtyping by circulating tumor DNA.”

MCL: Novel treatment options

#754: KTE-X19, an Anti-CD19 Chimeric Antigen Receptor (CAR) T Cell Therapy, in Patients (Pts) With Relapsed/Refractory (R/R) Mantle Cell Lymphoma (MCL): Results of the Phase 2 ZUMA-2 Study



Professor Martin Dreyling

“This phase II study using a CAR T-cell approach in MCL, has shown even better PFS than in DLBCL, with durable remissions even in high-risk patients, and could represent a new standard of care for patients with high-risk relapsed MCL.”



Doctor Astrid Pavlovsky

“R/R MCL is generally a devastating situation, with most patients dying of progressive disease. This experience, with 28 patients with R/R MCL, shows very promising rates of CR, DOR, EFS, and OS, offering CAR T-cell to a set of patients with otherwise limited options.”

[What are the promising updates in lymphoma at ASH 2019?](#)

[Results from the phase II ZUMA-2 trial: CAR T therapy for MCL](#)

[KTE-X19 receives CHMP positive opinion for the treatment of patients with R/R MCL](#)

#1530: Ibrutinib, Venetoclax Plus Obinutuzumab in Newly Diagnosed Mantle Cell Lymphoma Patients



Doctor Astrid Pavlovsky

“This is the first trial in reporting results with this triple combination for first-line MCL. Further follow-up is needed to compare this outcome *versus* other established therapies.”

[Results from the Oasis phase I/II trial on ibrutinib, venetoclax plus obinutuzumab in patients with newly diagnosed mantle cell lymphoma](#)

#756: Three Year Update of the Phase II ABT-199 (Venetoclax) and Ibrutinib in Mantle Cell Lymphoma (AIM) Study



Professor Martin Dreyling

“In aggressive, relapsed disease, the results of the Australian trial show that the combination of ibrutinib and venetoclax produces long-term remission with no plateau.”

[Practice-changing abstracts in MCL from ASH 2019](#)

FL: Chemotherapy-free treatment options

#347: Subgroup Analyses of Elderly Patients Aged \geq 70 Years in AUGMENT: A Phase III Randomized Study of Lenalidomide Plus Rituximab (R²) vs Rituximab Plus Placebo (R-Placebo) in Patients with Relapsed/Refractory (R/R) Indolent Non-Hodgkin Lymphoma (iNHL)



Professor Gilles Salles

“AUGMENT results show sustained efficacy and tolerability in older patients... we are learning how to use established drugs better.”

[AUGMENT: Is the combination of lenalidomide & rituximab efficacious in elderly patients with iNHL?](#)

[EMA approval of lenalidomide plus rituximab for adult patients with R/R FL](#)

#123: Phase 2 Multicenter Study of Tazemetostat, an EZH2 Inhibitor, in Patients with Relapsed or Refractory Follicular Lymphoma



Professor Gilles Salles

“Tazemetostat could be practice-changing for those patients who have failed previous lines of therapy.”

[Phase II study update of tazemetostat in patients with relapsed/refractory follicular lymphoma](#)

[Tazemetostat receives FDA Supplemental New Drug Application approval for adult patients with relapsed/refractory follicular lymphoma](#)

Treating patients with newly diagnosed CLL

#35: Ibrutinib (Ibr) Plus Venetoclax (Ven) for First-Line Treatment of Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL): Results from the MRD Cohort of the Phase 2 CAPTIVATE Study



Professor Susan O'Brien

“This is the second trial (MD Anderson data recently published in NEJM) showing very high MRD undetectability rates with the combination of ibrutinib and venetoclax— over 70% in both peripheral blood and marrow.”



Doctor Astrid Pavlovsky

“In the last years, we have witnessed a great improvement in the treatment of untreated or relapsed CLL with both ibrutinib and venetoclax. High efficacy with tolerable toxicity has been demonstrated with both drugs. The challenge remains in finding the best combination regarding efficacy, toxicity, and duration of treatment. The combination of ibrutinib and venetoclax aims to achieve high levels of undetectable MRD in a fixed-duration treatment. In this trial with ibrutinib and venetoclax, nearly all patients achieved response by the iwCLL criteria, with 93% uMRD. Although myelotoxicity is far less than the established treatment with chemo-immunotherapy, 20% of the patients discontinued due to AE. This treatment option could certainly become a new standard for frontline. Nevertheless, longer follow-up is necessary to evaluate the prognostic value for PFS of uMRD and if one year of treatment is enough for patients with ALL, or only for those with uMRD at the end of 12 months. Prognostic factors may help identify which patients this limited-time treatment yields better outcomes than continuous ibrutinib, longer venetoclax treatment, the addition of anti-CD20 antibodies or even the well-established treatment with FCR in young patients with mutated CLL.”

[Update from EHA 2020: Targeted therapy in CLL](#)

[Update on CLL induction therapy](#)

#33: Ibrutinib and Rituximab Provides Superior Clinical Outcome Compared to FCR in Younger Patients with Chronic Lymphocytic Leukemia (CLL): Extended Follow-up from the E1912 Trial



Professor Ulrich Jager

“This trial shows a survival advantage for ibrutinib + R in young patients with untreated CLL. Remarkable!”

[European approval for ibrutinib plus rituximab for frontline therapy in CLL](#)

#31: ELEVATE TN: Phase 3 Study of Acalabrutinib Combined with Obinutuzumab (O) or Alone Vs O Plus Chlorambucil (Clb) in Patients (Pts) with Treatment-Naive Chronic Lymphocytic Leukemia (CLL)



Dr Francesc Bosch

“In this randomized clinical trial, the new BTKi acalabrutinib, is compared alone or combined with obinutuzumab against the standard of care for patients with CLL and comorbid conditions. As in other similar studies, treatment with the BTKi proved to be superior to the standard chemoimmunotherapy combination. One of the important remarks of the study is that the combination of acalabrutinib plus obinutuzumab appears to obtain a better progression-free survival than acalabrutinib alone, pointing out that the addition of an anti-CD20 to these new drugs is, in some settings, beneficial.”

[Results from the phase III ELEVATE TN trial in patients with treatment-naïve chronic lymphocytic leukemia](#)

[Acalabrutinib for untreated CLL: delving into ELEVATE TN phase III trial results](#)

[What has the presentation of the ELEVATE TN trial taught us?](#)

Treating patients with R/R CLL

#502: Efficacy of Therapies Following Venetoclax Discontinuation in CLL: Focus on B-Cell Receptor Signal Transduction Inhibitors and Cellular Therapies



Professor Susan O'Brien

“Previously, there were little data on efficacy outcomes in patients receiving venetoclax and then going on to be treated with ibrutinib; this presentation had the largest cohort reported so far—44 patients who had high response rates and durable remissions. It’s very reassuring to know that ibrutinib is a great option in patients developing resistance to venetoclax.”



Doctor Constantine Tam

“It confirms that BTKi are effective in patients who fail VEN. Prior to this, we knew that VEN is effective after BTKi failure, but there was little information about the reverse order.”



Doctor Astrid Pavlovsky

“Treatment after venetoclax failure has become a new challenge in the treatment of CLL, especially due to the fact that most patients receive venetoclax in a relapse setting and after failure or intolerance to ibrutinib. In this trial, most patients had R/R CLL and had been exposed to 1–3 prior lines of treatment. This retrospective experience provides reassurance of using venetoclax prior to ibrutinib and supports the use of BTKi after venetoclax resistance in those with no prior exposure to BTKi; allogeneic transplant should also be considered in this setting. The importance of this experience is that it supports the use of venetoclax early in the course of CLL.”

Management of patients with CLL after venetoclax discontinuation

WM: Role of maintenance therapy

#343: Two Years Rituximab Maintenance Vs. Observation after First Line Treatment with Bendamustine Plus Rituximab (B-R) in Patients with Waldenström’s Macroglobulinemia (MW): Results of a Prospective, Randomized, Multicenter Phase 3 Study (the StiL NHL7-2008 MAINTAIN trial)



Professor Irene Biasoli

“The results of this trial showed no benefit of maintenance treatment with rituximab in terms of PFS and OS. Although the results of this study are negative, it highlights the importance of running randomized clinical trials in order to incorporate new strategies.”



Professor Judith Trotman

“In this large population of patients, the failure to identify a significant PFS advantage from rituximab maintenance after B-R induction for WM confirms the importance of randomized trials of maintenance across all indolent histologies. Given the additional infectious toxicity of maintenance with rituximab in WM, these data confirms the appropriateness of limiting first-line treatment with B-R to induction therapy only.”



Doctor Astrid Pavlovsky

“These results add to the growing body of evidence that rituximab maintenance is beneficial only in follicular lymphoma.”

Educational theme: Advances in treating Waldenström’s macroglobulinemia

Treating patients with poor-prognosis NHL

#6: Mosunetuzumab Induces Complete Remissions in Poor Prognosis Non-Hodgkin Lymphoma Patients, Including Those Who Are Resistant to or Relapsing After Chimeric Antigen Receptor T-Cell (CAR-T) Therapies, and Is Active in Treatment through Multiple Lines



Professor Ulrich Jager

“Will change practice also for post CAR T-cell treatment!”

Results from a phase I/Ib dose-escalation study of mosunetuzumab in high-risk non-Hodgkin lymphoma patients

FDA grants breakthrough therapy designation to mosunetuzumab for the treatment of adult patients with R/R follicular lymphoma

#4037: Imatinib +/- Brentuximab Vedotin Induces Sustained Complete Remission in Chemotherapy-Resistant Anaplastic Large Cell Lymphoma Expressing PDGFR



Professor Ulrich Jager

“Here, I take the freedom of mentioning an abstract from my own group describing long-term rescue of patients with ALCL unresponsive to chemotherapy with imatinib (and brentuximab vedotin).”

Brentuximab vedotin plus CHP is approved by the European Commission and China for the treatment of adult patients with sALCL

Educational theme: Advances in T-cell lymphomas



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