PERSPECTIVES ON THE TREATMENT OF MANTLE CELL LYMPHOMA AND FOLLICULAR LYMPHOMA IN 2015 AND BEYOND

Summary of presentations from the Celgene satellite symposium, held at the 20th Congress of the European Hematology Association (EHA), Vienna, Austria, on 11th June 2015

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MEETING SUMMARY

Prof Martin Dreyling opened the symposium by providing an overview of the current status of mantle cell lymphoma (MCL) and the current guidelines for treatment. Prof Steven Le Gouill discussed emerging tools to improve the diagnosis and monitoring of patients such as the assessment of minimal residual disease and the optimal incorporation of new technologies into the treatment pathway. Prof Marek Trněný then spoke about new treatment options for MCL and the improved survival that has been reported from certain combination therapies. Prof Martin Dreyling closed the MCL session.

Prof Gilles Salles introduced the follicular lymphoma (FL) session by explaining how the treatment landscape of FL has recently changed with the advent of anti-CD20 therapies. Prof Paulo Corradini then described the current treatment landscape in FL and Dr Jehan Dupuis spoke about the use of positron emission tomography (PET) at the start, interim, and end of treatment for FL. Prof Gilles Salles described the challenges of incorporating new treatment recommendations and tools for FL within current treatment options, and then summarised and closed the event.

Session 1: Managing Patients with Relapsed and/or Refractory Mantle Cell Lymphoma: Exploring Practical Solutions to Current Challenges

Welcome and Introduction

Professor Martin Dreyling

Prof Dreyling welcomed attendees to the meeting and outlined the challenges in MCL. MCL is a complex, heterogeneous disease that has classical, indolent, and transformed subtypes. Classical MCL constitutes the majority subtype and shows initially high response rates but relapses are also common. Indolent MCL occurs in 10–20% of patients, while 5–10% of patients with MCL have the transformed or blastoid subtype, which can be a difficult disease to treat successfully.

The Current Treatment Landscape in Mantle Cell Lymphoma: Current Guidelines and Remaining Challenges

Professor Martin Dreyling

MCL is a multifaceted disease that has previously been difficult to identify and treat. However, recent advances in the field have shown encouraging results with successes in the diagnosis and treatment of MCL. Only one-third of MCL cases can be accurately diagnosed using histological methods[1] and recent advances have enabled a confirmatory diagnosis of the t(11;14) chromosomal translocation that results in the overexpression of cyclin D1.[2] The indolent subtype of MCL can then be identified by t(11;14) translocation but no additional alterations, while classical MCL will also show impairment of DNA repair through ataxia telangiectasia mutated (ATM) and checkpoint kinase 2 (CHK2), as well as subsequent alterations. Transformed or blastoid subtypes show high levels of the Ki67 antigen, specific alterations in the *p53* tumour suppressor gene, and clinical features that can be evaluated through the Mantle Cell Lymphoma International Prognostic Index (MIPI). A study that stratified patients according to high, medium, or low risk by age (< or >65 years) and by the combined MIPI-c reported a significant difference in overall median survival between the high and low-risk groups ($p<0.0001$).[3]

Treatment decisions are then made according to the age of the patient, with dose intensification used for younger patients and maintenance regimenns for older patients.[4] Patients ≤65 years should be treated with dose-intensified immunochemotherapy (IC) using an alternating regimenn of three rounds of rituximab plus cyclophosphamide, doxorubicin, vincristine, prednisolone (R-CHOP) and rituximab plus dexamethasone, cytarabine, cisplatin (R-DHAP) regimenns as first-line treatment. An autologous stem-cell transplantation (ASCT) should be performed after the fourth course if there is no response, at which point total body irradiation, cytarabine (Ara-C), and melphalan should be used and then peripheral blood stem-cell transplantation (PBSCT) as the last action. Continued patient monitoring and follow-up is important to assess the recurrence of MCL. Long-term evaluation of patients treated with the regimenn demonstrated a 20% benefit of progression-free survival (PFS) after 10 years with the alternating R-DHAP regimenn versus the standard R-CHOP course.[5]

Patients >65 years should be initially treated with R-CHOP or rituximab conventional regimenns and then rituximab maintenance,[6] which has been shown to have significant benefits for PFS and overall survival (OS) in patients over a period of 10 years versus a maintenance phase with interferon or no maintenance treatment. The treatment strategy has subsequently become a standard treatment pathway for patients >65 years across most European countries.[6] Although there are set regimenns for the first-line treatment of patients with MCL, relapsed or refractory MCL can be aggressive and difficult to treat successfully due to the multiple pathways that are activated.[7] Newly available therapies include bortezomib, ibrutinib, temsirolimus, and lenalidomide and have been investigated in various studies as shown in Figure 1.[8–15] Ibrutinib plus rituximab treatment has shown overall response rates (ORRs) of 100% (n=34) in a single-centre Phase II study for patients with relapsing remitting MCL who do not show active cell proliferation (Ki67 <50%); however, for patients with active proliferation as indicated by a Ki67 ≥50%, the response rate dropped to 50%.[16] Therefore, treatment combinations may be required for the more aggressive types of MCL that show a Ki67 ≥50%. For example, the TRIANGLE study evaluated the effect of alternating R-CHOP and R-DHAP regimenns followed by ASCT with ibrutinib in patients ≥65 years.[17] In summary, a greater understanding of the MCL cellular

pathways has enabled the development of tools to provide an accurate diagnosis, while novel treatments have been shown to improve the overall and PFS rates of patients with MCL. Future studies are required to assess the efficacy and safety of combination treatments with the new agents.

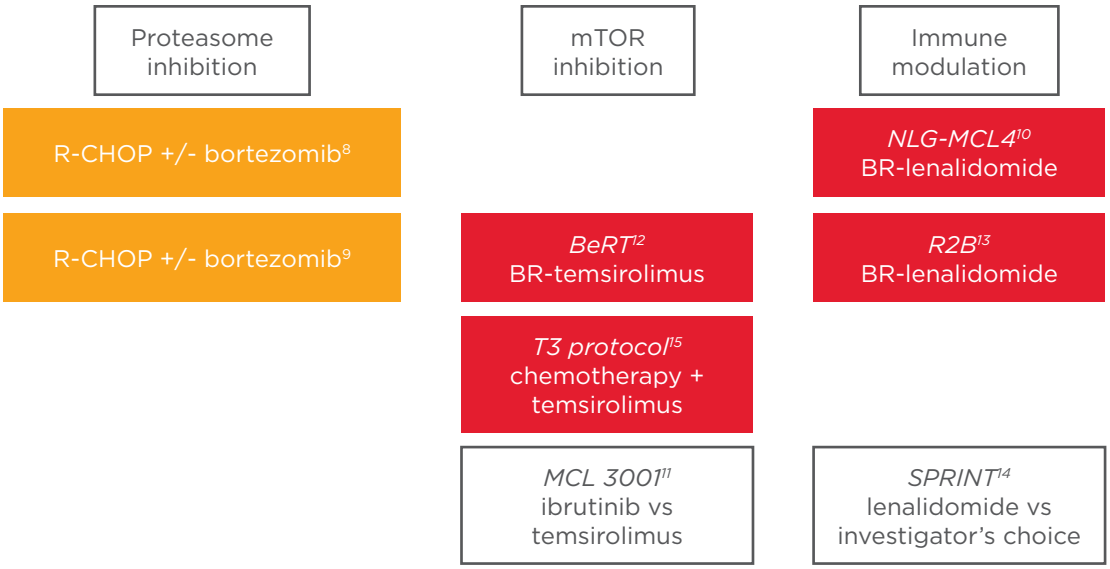

Figure 1: Mantle cell lymphoma studies 2015.[8-15]

From Martin Dreyling, presentation at the Celgene satellite symposium, held at the 20th Congress of the European Hematology Association (EHA), Vienna, Austria, on 11th June 2015.

BR: bendamustine plus rituximab; R-CHOP: rituximab plus cyclophosphamide, doxorubicin, vincristine, prednisolone; R-HAD: rituximab plus high-dose cytarabine and dexamethasone; mTOR: mammalian target of rapamycin.

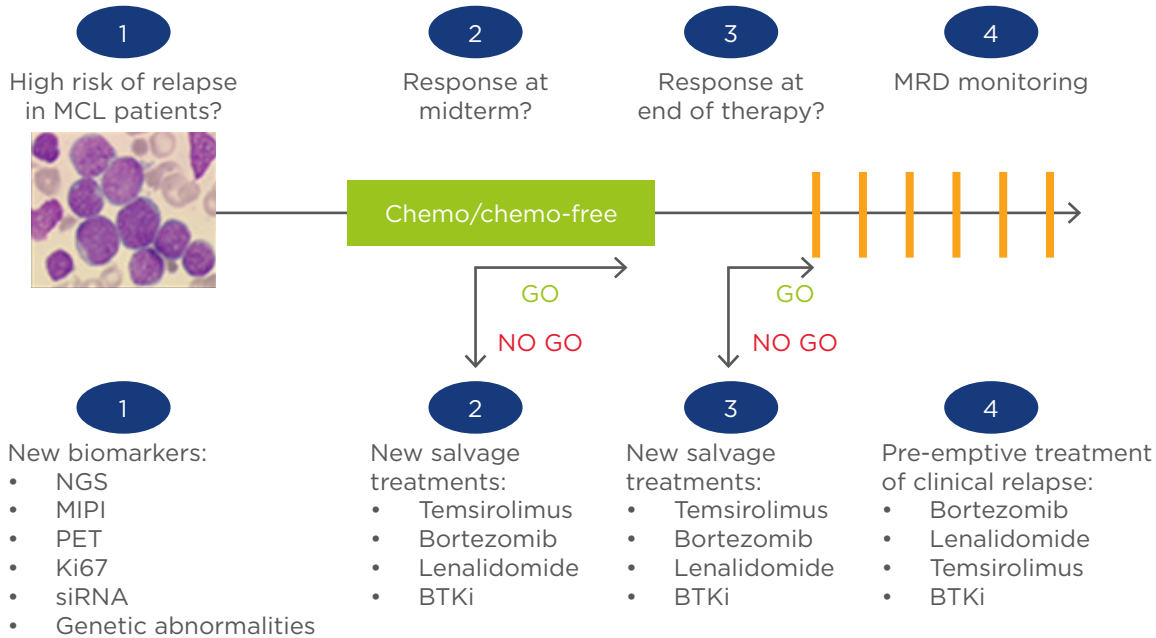

Figure 2: How to use new tools in a risk-adapted targeted strategy over time.

From Steven Le Gouill, presentation at the Celgene satellite symposium, held at the 20th Congress of the European Hematology Association (EHA), Vienna, Austria, on 11th June 2015.

BTKi: Bruton tyrosine kinase inhibitor; MCL: mantle cell lymphoma; MIPI: Mantle Cell Lymphoma International Prognostic Index; MRD: minimal residual disease; NGS: next-generation sequencing; PET: positron emission tomography; siRNA: small interfering RNA.

Emerging Tools for Driving Mantle Cell Lymphoma Treatment

Professor Steven Le Gouill

Along with the availability of new treatments for MCL, tools are currently being evaluated to ensure treatments are administered in the optimal setting to patients who have the highest probability of treatment response. These tools include the assessment of minimal residual disease (MRD) through flow cytometry, polymerase chain reaction (PCR), and real-time quantitative PCR (RQ-PCR), and there are advantages and disadvantages associated with each technique.[18] Although flow cytometry is well known and used, currently there are no standards or optimal settings for this technique in MCL and further validation studies are required prior to its use in routine practice. Comparatively, RQ-PCR has been standardised for MCL, however there is a low availability of this tool in laboratories. PCR is readily available and standardised, analyses of the IGH gene arrangement are detectable in 80–95% of B cell malignancies and the technique provides a short turnover time; however, there is a contamination risk with PCR and the data are qualitative, so interpretation of results is subjective.[18]

Although new treatments have been shown to induce remission in certain patients with MCL, confirmation is required on how, where, and when to evaluated the success of treatment regimenns. The LyMa trial, which recruited 299 patients and evaluate Ara-C (R-DHAP), analysed the MRD of patients prior to and after treatment (n=199). While all patients were high-level positive at the start of treatment, 65% of patients were MRD-negative after induction treatment and 79% were MRD-negative after ASCT treatment.[19] Another study by Pott et al.[20] reported maintained remission at 2 years in the majority of both younger and older patients who showed MRD negativity in peripheral blood and bone marrow samples compared with MRD-positive patients ($p<0.05$, n=259).[20] Remission shown through MRD negativity is a strong predictor of MCL prognosis, with MRD-negative patients demonstrating significantly improved PFS at 92 months ($p<0.001$, n=14) and OS at study end ($p<0.003$) versus MRD-positive patients (n=13).[21]

While the correlation of MRD with remission and improved PFS and OS has been confirmed, the appropriate use of MRD in routine clinical practice still requires verification and the optimal use, timing, and practicalities of MRD are still being studied. MRD can be evaluated upon diagnosis, at treatment interim prior to ASCT, at the end of treatment, and during follow-up. MRD can be assessed through the bone marrow tissue or blood. Although the use of blood to evaluate MRD is less invasive, confirmatory studies are required to compare blood versus bone marrow samples and the effect on patient outcomes. However, MRD is a promising future assessment tool that may minimise further treatment regimenns in patients who show MRD negativity during midterm treatment.

Another promising tool to evaluate the efficacy of treatment for MCL is fluorodeoxyglucose-PET (FDG-PET). Although the use of FDG-PET upon diagnosis is the current gold standard for nodal lymphomas and can be informative for MCL, so far there have been no studies or outcomes from using FDG-PET to optimise the patient treatment plan. FDG-PET can also be used for response assessment to ensure complete remission, but there are limitations of imaging certain areas such as the gastrointestinal tract, while the use of FDG-PET during follow-up is still undergoing experimental studies and requires validation as the false-positive rate with PET scans is over 20%.[22] There are also questions regarding the timing and use of FDG-PET. Although FDG-PET could be a promising technique in MCL, further studies are required to optimise its use for patients to ensure accurate imaging at an appropriate time in the treatment pathway.[22]

In addition to the diagnostic and imaging tools described above, it may be possible to tailor treatment according to the dysregulation of certain pathways in MCL through the use of '-omics'. There are multiple cellular processes that can be dysregulated in MCL that fall under three main areas, namely the NF-κB pathway, PIM1/mammalian target of rapamycin pathway, and epigenetic modifiers.[23] With genomic and proteomic techniques and novel treatments, it will be possible to tailor treatment according to which pathways or genetic processes are dysregulated and therefore target drugs according to the malfunction involved in MCL.

New techniques and modalities will allow the initial staging of patients with MCL to be refined through PCR techniques and FDG-PET so that treatment may be tailored according to the dysregulated pathways as shown by biomarkers. Evaluation of

treatment success via MRD and FDG-PET could show whether a change of treatment is required or not, as illustrated in Figure 2. The follow-up of patients will also be challenging; although new tools will provide the basis for physicians to determine whether treatment should be initiated, i.e. for MRD-positive patients who have not yet relapsed, these promising modalities will be complex and costly to bring into routine practice.

New Treatment Options for Mantle Cell Lymphoma on the Horizon

Professor Marek Trněný

There have been successes with new therapies in improving the outcomes of first-line treatment of MCL using a combination of approaches; however, there are still challenges with the relapsing or refractory forms of MCL. Real-life data report the probability of survival at 6 months as 50% for patients who are relapsing for the second or third time.[24] Therefore, novel treatments that target different points of the dysregulated pathways in MCL are being added on to existing therapies for relapsing patients and include temsirolimus, bortezomib, ibrutinib, and lenalidomide plus other investigational drugs such as ABT-199. In addition to targeting the pathways involved in MCL, the micro-environment and immune-regulation also play an important role in the evolution of MCL, and agents such as lenalidomide and ibrutinib can be used to improve the OS and PFS of patients with MCL.[25,26]

Recent treatments that have shown promising results in relapsed refractory MCL include temsirolimus, bortezomib, ibrutinib, and lenalidomide. Recent Phase III data on temsirolimus showed an ORR of 22% and a median PFS of 4.8 months as an individual agent (n=162).[27] When combined with rituximab and bendamustine, further improvements were seen in ORR (91%, n=11).[12,27,28] Bortezomib reported an ORR of 33% and median PFS of 6.2 months as an individual agent in patients with relapsed/refractory MCL (n=155),[29] and the addition of dexamethasone demonstrated increases in ORR and PFS to ˜80% and 12 months, respectively (n=16).[30,31] Recent studies have shown benefits in combination therapy for induction treatment, with bortezomib and rituximab plus cyclophosphamide, doxorubicin, and prednisone demonstrating superior PFS of 24.7 months (133 events) versus standard R-CHOP treatment that reported a PFS of 14.4 months (p<0.001, 165 events).[8] Ibrutinib inhibits Bruton's tyrosine kinase and has shown an ORR of 67% and median PFS of 13 months as an individual agent (n=111),[32,33] with an ORR of 87% and complete response of 38% when combined with rituximab (n=45).[16] In a Phase II study, duration of response was 17.5 months from a median follow-up of 26.7 months and patients showed an OS of 22.5 months. Ibrutinib demonstrated a good toxicity profile but has certain contraindications.[32,33]

Lenalidomide has demonstrated positive outcomes from studies as both a single agent and when combined with other treatments for patients with relapsed or refractory MCL.[34–39] The ORR is approximately 30% when prescribing lenalidomide alone, with Trněný et al.[36] reporting a PFS of 8.7 months (p=0.004) and ORR of 40% (p<0.001), with a median follow-up of 15.9 months (n=170).[36] The control arm was investigators' treatment choice, which reported a PFS of 5.2 months and ORR of 11% and more than half of these patients were switched to lenalidomide upon relapse. Manageable safety was reported, with mainly haematological toxicities observed. When lenalidomide was used in combination with rituximab, the ORR increased to approximately 55% and PFS to approximately 15%.[34,38,39]

Overall, the ORR of targeted therapies for patients with relapsed or refractory MCL varies from 20-65% and median PFS is between 5 and 13 months, whereas the duration of response is up to 17 months and OS between 13 and 28 months.[27,29,32,36] However, challenges remain in determining the optimal treatment combination for relapsed or refractory patients with MCL and which chemotherapy regimenns should be used, if at all.[40] Promising combinations that are undergoing clinical trials include lenalidomide plus ibrutinib,[41] rituximab plus lenalidomide plus ibrutinib,[42] obinutuzumab plus lenalidomide,[43] rituximab plus lenalidomide plus carfilzomib,[44] ABT-199 plus ibrutinib,[45] and ibrutinib plus palbociclib.[46]

In conclusion, new treatment modalities have already shown significant improvements in patients with relapsed or refractory MCL. Future directions for therapies will include combination treatment with and without chemotherapy, with targeted treatment moving to an earlier phase of disease that includes first-line treatment.

Closing Remarks for the MCL Session

Professor Martin Dreyling

Advances in the diagnosis of MCL have improved the accuracy of recognising and treating the disease. Although molecular markers are required to tailor treatments to the disease characteristics of each patient, future opportunities will be to utilise the available treatments and tools to develop and refine therapeutic algorithms and treatment combinations for patients.

Session 2: Shaping the Landscape in Follicular Lymphoma: How New Approaches will Guide Future Treatment Options

Introduction

Professor Gilles Salles

Treatment options and outcomes of patients with FL have drastically improved over the past 20 years, thereby requiring changes to the treatment pathways. In 1960, the OS of patients with FL was unchanged despite available treatments, with a median survival of around 8–10 years.[47,48] Although these treatments show benefits and can still be used, careful selection of therapies to minimise side-effects and include novel treatments is required. The limitations of classical cytotoxic therapies are cumulative toxicities that can result in the contraindication of these treatments in certain patients. Single-agent rituximab can be used as an alternative, non-cytotoxic method of effectively treating certain patients with FL,[49] as well as other novel agents.

Due to the availability of anti-CD20 antibodies, treatment options have expanded and an improved median survival of around 15–18 years in patients with FL has been reported.[50,51] Anti-CD20 therapies should be evaluated using different treatment combinations in order to maximise their benefit by investigating the therapies in single-arm studies, to be further confirmed in controlled trials. Due to the changing landscape of FL, new endpoints need to be defined that will provide a more informative basis by which treatment decisions are made as well as for the monitoring and follow-up of patients.[52] The availability of new and efficacious therapies requires a rethink of established endpoints and studies should therefore use a range of methods to evaluate clinical outcomes.

High Tumour Burden Follicular Lymphoma: The Current Treatment Landscape

Professor Paolo Corradini

Although there is a range of newly available therapies that have shown improved survival in patient studies, these should be used alongside established therapies in order to maximise clinical outcomes. Current treatments centre on radiotherapy, watch and wait, IC, ASCT, radioimmunotherapy (RIT), and allogeneic transplantation (ATx) for patients who relapse after ASCT.[53] Upon diagnosis of FL, the main treatments are R-CHOP, rituximab plus cyclophosphamide, vincristine, and prednisone (R-CVP) and rituximab plus fludarabine and mitoxantrone (R-FM). The 3-year FOLL05 study[54] evaluated over 500 patients for 3 years and reported significantly improved time to treatment failure with R-CHOP (p=0.003) and R-FM (p=0.006) regimenns compared with the R-CVP treatment. Additionally, bendamustine plus rituximab (B-R) is a novel treatment that has shown non-inferiority to the R-CHOP regimenn across two studies with an acceptable safety profile and fewer toxic effects.[55,56] Although maintenance treatment with bendamustine still needs to be evaluated, three options of R-CHOP, R-FM, and B-R are now available to treat patients upon diagnosis of FL. Other promising therapies include rituximab maintenance treatment, which showed improved PFS versus standard treatment.[57,58] RIT has also reported promising results, with a 100% ORR in patients given a single infusion of irradiated ibritumomab tiuxetan as initial therapy (n=17).[59]

After the initial treatment, ASCT is an option for patients who have relapsed. Guidance states that ASCT is not appropriate to consolidate the first remission in FL responding to IC treatment outside of clinical trials. ASCT is recommended for patients with a short treatment response, duration (<3 months), a high-risk Follicular Lymphoma Prognostic Index (FLIPI) score at relapse and for those previously treated with rituximab.[60] ASCT is also an option at second or subsequent relapse in chemotherapy-sensitive patients, and the decision to use ASCT should be governed by the clinical

course rather than biological and genetic risk factors. Cabanillas et al.[61] reported long-term follow-up of patients with FL who received ASCT and found improved survival of patients who received high-dose cyclophosphamide and total-body irradiation prior to ASCT during the second remission versus a historical control group treated with conventional chemotherapy. Purging with rituximab prior to ASCT does not appear to improve survival;[62] however, the study may have been under-powered. Patients who relapse after the first-line treatments and then also post-ASCT can present a challenge to treat successfully. Allogeneic stem cell transplantation has shown positive results in patients who have failed ASCT when bendamustine was replaced with fludarabine, with improved PFS and OS after 36 months.[63,64]

Along with a greater range of efficacious treatments, improved tools to monitor the progression of patients should be implemented for FL as per other malignancies. Reports have shown that molecular remission as demonstrated by PCR-negative status occurs in a greater proportion of FL patients.[65,66] Therefore, MRD techniques should be integrated into the definition of patient response for FL. In summary, the R-CHOP, R-CVP, and B-R regimenns have shown good outcomes for first-line therapy, while patients who relapse should be considered for ASCT and then allogeneic ATx if subsequent relapses occur. New therapies show promise for FL, however trials need to be carefully designed in order to fully evaluate all treatment options.

The Role of Positron Emission Tomography in Guiding Treatment Options

Doctor Jehan Dupuis

The implementation of novel treatment options requires careful monitoring in order to ensure that the optimal treatment regimenn is given to patients. The imaging modality PET may be a useful tool to ensure correct diagnosis and monitoring, as the technique detected additional lesions in 32% of patients who participated in the FOLL05 study[67] compared with computed tomography (CT) (n=142). Furthermore, of the patients who had initially been diagnosed with radiotherapy for localised disease by CT, 62% of cases were upstaged upon PET examination.[67,68]

The use of PET prior to treatment initiation has been recommended by the International Harmonization Project guidelines in order to interpret the PET results after treatment completion.[69] However, it should be noted that PET imaging cannot replace the use of bone marrow biopsies to assess for transformations but should be used as an additional tool.[67] The use of PET during treatment has not been reported widely, however a study that assessed the use of PET during and after treatment found that end-of-treatment PET is more predictive of outcomes.[70] Therefore, current evidence suggests that the use of PET in the middle of treatment is not recommended (Courtesy of LYSARC). The use of PET after treatment to evaluate treatment success appears to be highly predictive of patient outcomes. Trotman et al.[71] reported a median survival of >6 years in PET-negative patients (n=205) according to the PET scan score versus 1.5 years in 41 PET-positive patients ($p<0.0001$). However, no interventional study based upon PET results has been conducted so far and rituximab maintenance remains the standard of care regardless of the post-treatment PET score.[58]

When transformation is suspected, the relative measure of local radiotracer accumulation in the tissues can be measured with PET using the standardised uptake value (SUV). SUV can vary with biological factors, the method of analysis, and image reconstruction parameters. Transformation should be suspected when a focus of more intense radiotracer uptake in the tissues is identified via PET.[72-74] Higher SUVs have been found to correlate with more aggressive histologies[72,73] and PET can be used to guide the choice of biopsy site, yet the predictions are not certain and therefore biopsies are still required. In conclusion, PET scans should be performed in patients with FL prior to and after treatment, and PET-positive patients should be monitored closely for disease progression.

Challenges for Shaping a New Paradigm of Care in Follicular Lymphoma

Professor Gilles Salles

There has been an evolution in the landscape of FL and recent findings need to be understood in order to optimise treatment pathways. The key events that lead to the development of lymphoma have been described but are not yet fully

understood.[75-77] However, there are standard treatment strategies for the various stages of FL. While the disease cannot be eliminated fully through cytotoxic therapy, the use of ASCT and ATx have shown success with rates of remission and the combination of existing therapies with novel agents may ensure improved PFS and OS in patients with a range of FL staging and severity. Novel agents include immune checkpoint inhibitors and immunomodulatory drugs, aiming to target the cancer stem cell in FL.[78] A recent trial of pidilizumab plus rituximab, which can be directed against PD-1 and/or PD-L1, was suggestive of efficacy in FL. However, as inclusion criteria required patients who were rituximab-sensitive, confirmatory studies are required.[79]

Through analysis of T cells within the FL microenvironment to understand the "immune tolerance" towards tumour cells in FL, reports have shown defects in the ability of T cells to kill the FL tumour cells.[80] Further *in vitro* studies have since indicated that lenalidomide may have a role in restoring the T-cell immune response so that FL cells are targeted by the T cells. Lenalidomide as a single agent or combined with rituximab in relapsing patients with FL has resulted in an ORR of 25–40% and 50–85%, respectively.[81-83] Improvements in CR have also been reported with lenalidomide + rituximab, as 30–50% of patients achieved CR when treated for relapsed or refractory FL.[84,85] Furthermore, Fowler et al.[86] assessed lenalidomide + rituximab in patients with untreated, advanced stage indolent non-Hodgkin lymphoma. The Phase II study from one institution reported an 87% complete response (n=40) of patients with FL. Safety monitoring during the study demonstrated Grade 3/4 neutropaenia incidence in 35–40% of these patients and rashes, myalgia, and thrombosis were also reported, indicating the need for monitoring of treatment side-effects.

From the encouraging PFS data shown with lenalidomide and rituximab, a trial that evaluated various treatment strategies with this combination dropped the single rituximab arm through demonstration of superiority of the combination treatment.[87] Significant improvements were then shown through the CALGB 50401 study (Table 1) across ORR and median event-free survival. Based upon promising results from the combined lenalidomide plus rituximab treatment, the international, multicentre, randomised study RELEVANCE[88] will evaluate standard treatments R-CHOP, R-CVP, and R-B versus lenalidomide + rituximab maintenance.

In closing, the data shown from new agents are changing the landscape of FL and improving outcomes for patients. Development of the immunotherapy approach, combination treatments, and new agents with rituximab could be very promising.

Table 1: Response and event-free survival: CALGB 50401 study.[87]

	Lenalidomide (n=45)	Lenalidomide + rituximab (R2) (n=44)
ORR, %	51.1 95% CI (35.8–66.3)	72.7 95% CI (52.2–85.0)
CR, %	13.3	36.4
PR, %	37.8	36.4
Median EFS (years)	1.2	2.0
2-year EFS, %	27	44

From Gilles Salles, presentation at the Celgene satellite symposium, held at the 20th Congress of the European Hematology Association (EHA), Vienna, Austria, on 11th June 2015.
Median follow-up: 1.5 years (range 0.1–3.6). Unadjusted EFS HR of lenalidomide vs lenalidomide + rituximab (R2) is 2.1 (p=0.010). Adjusted (for FLIPI) EFS HR of lenalidomide vs lenalidomide + rituximab (R2) is 1.9 (p=0.061).
CALGB: Cancer and Leukemia Group B; CI: confidence interval; CR: complete response; EFS: event-free survival; FL: follicular lymphoma; FLIPI: Follicular Lymphoma International Prognostic Index; HR: hazard ratio; NHL: non-Hodgkin lymphoma; ORR: overall response rate; PR: partial response.

Closing Remarks for the Follicular Lymphoma Session

Professor Gilles Salles

While the development of novel agents has been met with intense interest from the FL community, long-term follow-up studies are needed to evaluate the potential benefit of novel agents in prospective clinical trials versus standard treatment. Additionally, the integration of novel tools such as MRD and PET-CT are required to support treatment decisions with novel agents as well as conventional therapies.

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