Lymphoma Tumor Board 2020

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Case 1

- 68 year old female with no past medical history who presented with shortness of breath
- Examination was unremarkable, no palpable lymphadenopathy noted
- Labs showed a WBC of 7.1 K/mm^3 with normal differential, Hb of 12.5 g/dL and Plt of 234 K/mm^3, CMP was unremarkable; LDH was 124 U/L
- PET/CT showed a 12 cm mediastinal and 2 cm retroperitoneal lymphadenopathy with SUV ranging from 18-20
- Excisional biopsy of the mediastinal lymphadenopathy showed CD30+, CD15+, CD20- classical Hodgkin lymphoma, nodular sclerosing subtype

Case 1

Patient was diagnosed with stage III Hodgkin lymphoma, IPS of 2. Assuming an ECOG of 0, what treatment would be the best option for this patient?

A. ABVD

B. AVD + Brentuximab

C. Escalated BEACOPP

D. Clinical Trial: AVD + Brentuximab vs. AVD + Nivolumab (S1826)

Case 1

Patient received ABVD therapy. PET/CT after 2 cycles showed mediastinal lymphadenopathy with Deauville score of 3 and retroperitoneal lymphadenopathy with Deauville score of 2. What is the best treatment option at this moment?

A. ABVD x4 cycles
B. ABVD x4 cycles with radiation to bulky site
C. AVD x4 cycles
D. AVD + Brentuximab x4-6 cycles
E. Escalated BEACOPP

Case 1

Patient received ABVD x4 more cycles with involved field radiation therapy to bulky mediastinal site with subsequent complete remission. 6 months later, patient presents with recurrent shortness of breath found to have relapsed disease localized to the mediastinum. What is the best treatment option at this moment?

A. ICE
B. Brentuximab
C. Pembrolizumab

Case 1

Patient received ICE. PET/CT after 2 cycles shows refractory disease. Therapy was changed to brentuximab with subsequent partial remission. Therapy was again changed to pembrolizumab with subsequent complete remission. What is the next best therapy at this moment?

A. Observation
B. Autologous SCT
C. Allogeneic SCT
D. Clinical trial

Hodgkin Lymphoma

- Bleomycin omission from ABVD after negative interim PET resulted in less pulmonary toxicity but not significantly lower efficacy when compared to continued ABVD (RATHL; Johnson 2016)
- Intensification with escalated BEACOPP after positive PET2 associated with good outcomes: 3-year PFS: 63% with Rituximab vs 57% without (GITIL/FIL HD 0607; Gallamini 2018)
- A+AVD associated with longer modified-PFS compared to ABVD in advanced-stage Hodgkin's lymphoma regardless of PET2 status (ECHELON-1; Connors 2018)
  - Analysis of North American subgroup support ECHELON-1 results (Ramchandren 2019)

Hodgkin Lymphoma

- Consolidative radiotherapy may be beneficial for advanced Hodgkin lymphoma with bulky disease: 3-year PFS 10.3% with radiation vs 7.5% without (HD0801; Ricardi 2019)
- SCT improves freedom from treatment failure but not overall survival in patients with chemosensitive 1st relapse of HD (Schmitz 2002)
- Brentuximab consolidation after autologous SCT for high risk Hodgkin lymphoma beneficial: 5-year PFS: 59% with Brentuximab vs 41% with placebo (AETHERA; Moskowitz 2018)
- 38% of patients with R/R Hodgkin lymphoma after failed autologous SCT who achieved complete response on brentuximab have remained in remission for >5 years; 9% without allogeneic SCT (Chen 2016)

End of Case 1

Case 2

- 55 year old male with no past medical history who presented with dysphagia associated with a lump on his neck which he first noted 6 months ago
- Examination revealed palpable cervical lymphadenopathy, otherwise unremarkable
- Labs showed a WBC of 10.8 K/mm^3 with normal differential, Hb of 11.4 g/dL and Plt of 265 K/mm^3, CMP was unremarkable; LDH was 122 U/L
- PET/CT showed a 6 cm left cervical lymphadenopathy, 7 cm mediastinal lymphadenopathy, left pleural mass and para-aortic lymphadenopathy SUV ranging between 6-8

Case 2

- Excisional biopsy of the cervical lymphadenopathy showed CD20+, CD10+ BCL2+, BCL6+ and CD5- follicular lymphoma, predominantly grade 3A on background of grade 1-2
- Patient was diagnosed with Stage IV follicular lymphoma, predominantly grade 3A

Case 2

Assuming an ECOG of 0, what treatment would be the best option for this patient?

A. Observation
B. Rituximab monotherapy
C. Bendamustine/Rituximab (BR) x6 cycles
D. BR with Rituximab maintenance
E. Lenalidomide/Rituximab (R^2)
F. R-CHOP

20th Multidisciplinary Management of Cancers: A Case-based Approach

Case 2

Patient received upfront BR chemotherapy x6 cycles with resolution of clinical symptoms. 2 years later, patient noted recurrent dysphagia with cervical lymphadenopathy. What treatment is indicated at this point?

A. Obinutuzumab/bendamustine
B. Lenalidomide/Rituximab (R^2)
C. Idelalisib +/- rituximab
D. Autologous SCT
E. PET scan and consideration of re-biopsy

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20th Multidisciplinary Management of Cancers: A Case-based Approach

Case 2

Patient received R^2 therapy with subsequent complete remission. 2 years later, patient noted to have relapsed disease. Patient then receives Idelalisib therapy with subsequent partial remission. What is the next best treatment at this point?

A. Continue Idelalisib until progression
B. Autologous SCT
C. R-CHOP
D. Blinatumomab/lenalidomide clinical trial at UCD
E. CAR-T clinical trial at UCSF

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20th Multidisciplinary Management of Cancers: A Case-based Approach

Indolent lymphomas

- BR non-inferior to R-CHOP while showing better tolerability profile for untreated follicular and mantle cell lymphoma (StiL; Rummel 2013)
- Rituximab maintenance after first-line immunochemotherapy improved PFS but not OS compared to observation in follicular lymphoma (PRIMA; Salles 2011)
- Rituximab/Revlimid (R^2) non-inferior to R-chemo while showing better tolerability profile for untreated follicular lymphoma (RELEVANCE; Morschhauser 2018)
- R^2 improved PFS compared to rituximab monotherapy in relapsed indolent lymphoma (AUGMENT; Leonard 2019)
- Autologous SCT associated with improved survival for POD24 in CR2: 5-year PFS: 51% with ASCT vs. 19% without (Jurinovic 2018)

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End of Case 2

Case 3

- 40 year old male with no past medical history who presented with lump in right groin and no other symptoms
- Examination revealed right inguinal lymphadenopathy, otherwise unremarkable
- Labs showed a WBC of 10.2 K/mm^3 with normal differential, Hb of 13.5 g/dL and Plt of 300 K/mm^3, CMP was unremarkable; LDH was 138 U/L
- PET/CT showed lymphadenopathy in retrocaval, right common iliac, right pelvic side wall and left external iliac areas as well as spleen, SUV between 6-8

Case 3

- Excisional biopsy of the cervical lymphadenopathy showed mature CD4$^+$/CD8$^-$ T-cells among a CD21$^+$ follicular dendritic-cell network with prominent arborizing high-endothelial venules; CD30 expression 15%
- Bone marrow biopsy showed no involvement of malignancy
- Patient was diagnosed with stage IV angioimmunoblastic T cell lymphoma

Case 3

Assuming an ECOG of 1, what treatment would be the best option for this patient?

A. CHOEP
B. Brentuximab monotherapy
C. Brentuximab + CHP
D. Lenalidomide
E. Praletrexate
F. Clinical trial

Case 3

Patient receives CHOEP therapy with subsequent complete remission (pre ECHELON-2 trial). Should patient be referred for stem cell transplantation at this time (CR1)?

A. Yes

B. No

Case 3

Patient underwent autologous SCT. 14 months later, patient noted drenching night sweats associated with weight loss. PET showing recurrent lymphadenopathy secondary to relapsed disease. What is the optimal treatment at this point?

A. Brentuximab monotherapy

B. Brentuximab + CHP

C. Lenalidomide

D. Belinostat

E. Tipifarnib clinical trial at Stanford

F. Nivolumab

Case 3

Patient received Brentuximab monotherapy with subsequent complete remission. What is the next best step?

A. Observation

B. Allogeneic SCT

C. CAR-T therapy on clinical trial at MD Anderson

D. Clinical trial

Angioimmunoblastic T-cell lymphoma

- Brentuximab + CHP showed longer PFS and OS compared to CHOP in untreated CD30+ PTCL; benefit seen with and without ASCT (ECHELON-2; Horwitz 2019)
- CHOEP associated with 3-year EFS of 50% and OS of 67.5% in AITL (Schmitz 2010)
- Dose-dense induction followed by HDT/ASCT was well tolerated and led to long-term PFS in 44% of treatment-naïve PTCL patients; rational up-front strategy in transplant-eligible patients (d'Amore 2012)
- Autologous SCT did not improved PFS compared to active observation in PTCL patients achieving CR1 following CHOP-like induction chemotherapy (Yam 2016)
- Brentuximab showed antitumor activity in relapsed/refractory AITL with ORR 54% (Horwitz 2014)

Angioimmunoblastic T-cell lymphoma

- Belinostat induced rapid and durable response with relapsed/refractory AITL (ORR 46%, CR 18%, median time to response 11.3 weeks) (Sawas 2019)
- Nivolumab for relapsed/refractory PTCL associated with ORR 33%, showed hyperprogressive disease in 33%, study halted (Bennani 2019)
- Allogeneic SCT provides durable disease control in relapsed/refractory AITL patients who failed a prior autologous SCT (4-year PFS: 21%) (Epperla 2019)
- Some ongoing clinical trials:
  - MEDI-570 in relapsed/refractory AITL, Tipifarnib in relapsed/refractory PTCL, CPI-818 in relapsed/refractory T-cell lymphoma

End of Case 3

Case 4

- 55 year old male with no past medical history who presented with a lump on his neck and drenching night sweats for the past 3 weeks
- Examination revealed right cervical and axillary lymphadenopathy, otherwise unremarkable
- Labs showed a WBC of 12.8 K/mm^3 with normal differential, Hb of 12.1 g/dL and Plt of 233 K/mm^3, CMP was unremarkable; LDH was 441 U/L
- PET/CT showed cervical, axillary, mediastinal and retroperitoneal lymphadenopathy, all with SUV of 11-13. In addition, hypermetabolic foci also noted in right scapula and posterior 8th rib

Case 4

- Excisional biopsy of the cervical lymphadenopathy showed diffuse large B-cell lymphoma, non-GCB subtype. Immunohistochemistry showed BCL2 80% and C-MYC 50%, Ki67 60%. BCL2, but no BCL6 or MYC gene arrangement was noted
- Bone marrow biopsy showed no evidence of lymphoma involvement
- Patient was diagnosed with stage IV DLBCL, non-GCB subtype, double expressor

Case 4

Assuming an ECOG of 0, what treatment would be the best option for this patient?

A. R-CHOP

B. R-CHOP with IT methotrexate

C. MR-CHOP

D. DA-R-EPOCH

E. DA-R-EPOCH with IT methotrexate prophylaxis

Case 4

Patient receives DA-R-EPOCH with IT methotrexate chemotherapy x6 cycles with subsequent complete remission. Should patient receive stem cell transplantation at this time?

A. Yes

B. No

Double-expressor lymphoma

- immunohistochemical overexpression of MYC >40% and BCL2>70%
- present in up to one-third of patients with DLBCL
- poor outcomes even after autologous SCT due to early disease progression (2 year PFS 20% with DEL vs 78% without DEL) (Herrera 2016)
- DA-R-EPOCH more toxic and did not improved PFS or OS compared to R-CHOP in untreated DLBCL; DEL subset insufficient size for statistical comparison (Alliance/CALGB 50303; Bartlett 2019).
- Clinical outcomes of DLBCL with overexpression of MYC and/or BCL2 treated with R-EPOCH may not be inferior in comparison to DLBCL with lack of overexpression (Issa 2016)
- CNS-IPI can be used to estimate CNS relapse/progression risk in DLBCL treated with R-CHOP (Schmitz 2016)

End of Case 4

Case 5

- 64 year old male with no past medical history who presented with weakness, weight lose and oozing of blood from gums
- Dental evaluation was unremarkable. Examination revealed hepatosplenomegaly, otherwise unremarkable.
- Labs showed a a WBC of 2.5 K/mm^3 with normal differential, Hb of 8 g/dL and Plt of 45 K/mm^3, CMP was unremarkable. IgM 4.5 g/dL, serum viscosity 5
- Bone marrow biopsy showed 20% infiltration by small lymphocytes that exhibit lymphoplasmacytic features and express IgM+, CD10-, CD19+, CD20+, CD22+, CD23-, CD25+, CD27+, FMC7+, CD103- and CD138-. MYD88 mutation positive consistent with Waldenstrom macroglobulinemia.

Case 5

Should patient receive therapeutic plasma exchange?

A. Yes

B. No

Case 5

Patient receives TPE with improvement in clinical symptoms. What treatment would be best for this patient at this moment?

A. Observation

B. Rituximab

C. Bendamustine alone until IgM reduced by ~50%, then BR

D. Bortezomib/Dexamethasone/Rituximab (BDR)

E. Dexamethasone/Rituximab/Cyclophosphamide (DRC)

F. Ibrutinib/Rituximab

Waldenstrom Macroglobulinemia

- incurable, low grade lymphoplasmacytic lymphoma characterized by the presence of IgM-secreting clonal cells in bone marrow, MYD88 mutation found in >90%
- DRC well tolerated and effective in untreated WM with ORR 83% (Dimopoulos 2007)
- BDR well tolerated and induced durable responses in untreated WM (Dimopoulos 2013)
- Ibrutinib/rituximab showed higher PFS than placebo/rituximab in untreated and relapsed/refractory WM (30-month PFS rate 82% vs 28%) (Dimopoulos 2018)
- Ibrutinib efficacious in relapsed/refractory WM with ORR 91% (Treon 2015)
- 54% of patients treated with rituximab may experience an IgM flare; most experience a decrease in IgM levels within 4 months after initiation of therapy (Ghobrial 2004)

End of Case 5