Mantle Cell Lymphoma
Case Presentation

Acknowledgement:
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65F JB

- Fit and well
- PMH -insomnia
- DH – temazepam, amitryptylline

- May 2018 - Presented with mass at base of tongue ?
  Histology: mantle cell lymphoma

MC: First line– 2018

Risk profile

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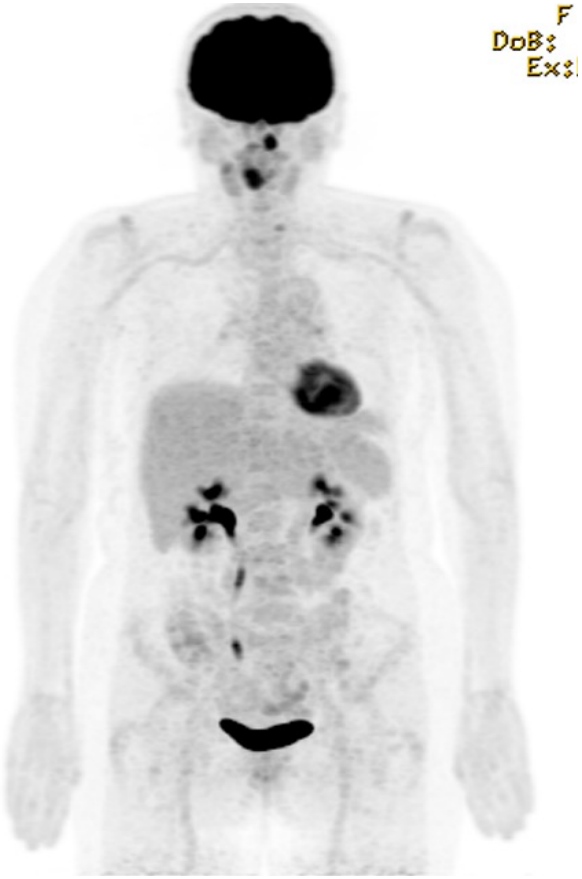
1. clinical stage
2. patient demographics/lab
3. histology
4. other

FDG-PET/CT



Features

- Right base of tongue lesion intense activity
- Left nasal cavity FDG avid opacification
- Right level IIA LN uptake
- Bilateral cervical LN mild uptake
- No other sites of disease
- →Stage IIA MCL

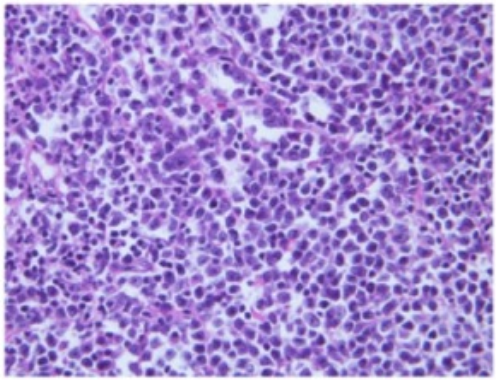
MIPI

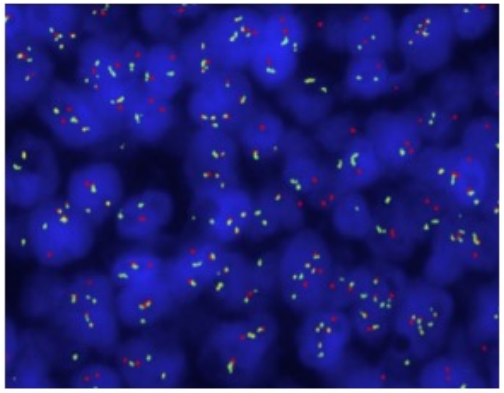
- Age → 65 years
- LDH→231 (250)
- WCC→6.26 x 10^9/L
- ECOG →0

Biopsy – mantle cell lymphoma

Biopsy

- Pleomorphic
- Ki67 80%
- CD20+, CD79a+, CD5+
- Cyclin D1 +, BCL2+
- FISH: Hemizygous P53 deletion
- NGS: No *TP53* mutation





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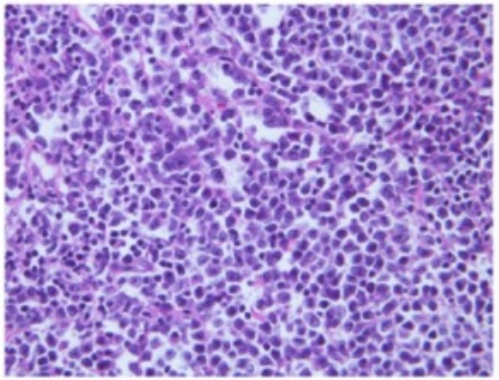

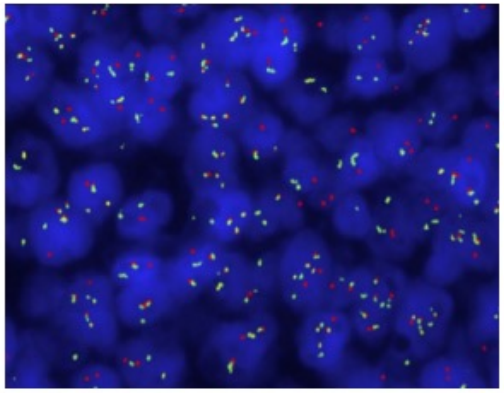

So far?

- 65F
- Fit and well
- Stage IIA mantle cell lymphoma
- MIPI = 6.6 (high risk; OS 37 months)
- Poor prognostic features
  - Pleomorphic morphology
  - Ki67>30%
  - Hemizygous TP53 deletion by FISH

Treatment options

- Transplant eligible?
  - She is

- BUT…..Is that the best approach?
- No rituximab maintenance
- ?BTK inhibitor frontline

MC: First line– 2018
optimal treatment

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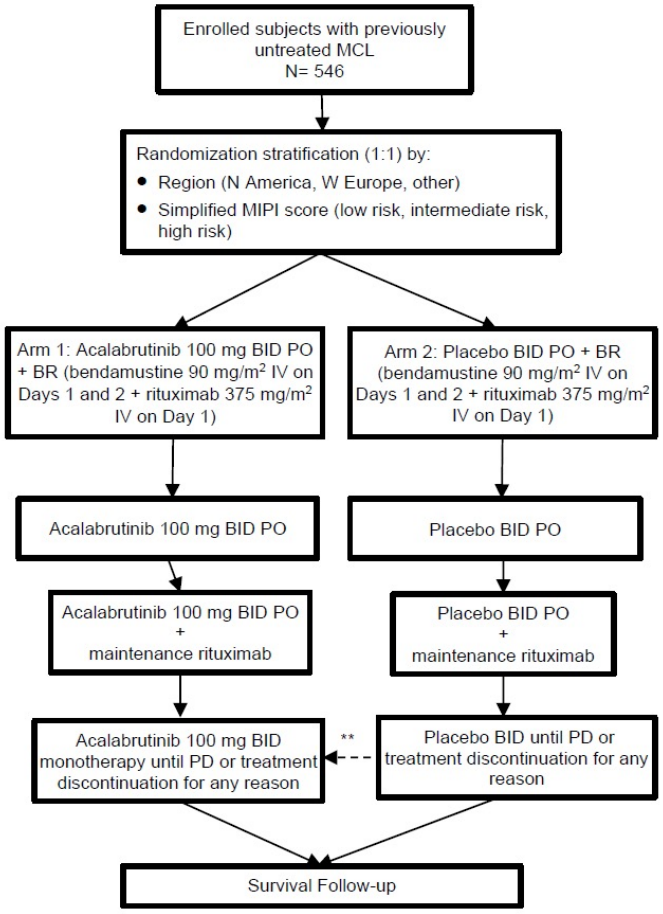
1. Intensive R-chemo/autologous SCT/R maintenance
2. BR
3. BTKi frontline
4. clinical trial

ACE-LY-308 trial



Treatment course

- Enrolled on ACE-LY-308
- BR plus acala/placebo (blinded)

- EOC3 – CR (CT)
- EOC6 – PD
  - -’large lipomatous pelvic mass’ – CT
  - Significant disease progression – FDG/PET

Next steps on trial

- Had she been receiving BTK inhibitor as part of her therapy so far?
- -If not – acalabrutinib on trial
- -If so – off trial and consider alternative therapy

- → randomised to acalabrutinib at study entry

First relapse - 2019

Optimal treatment

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1. R-CHOP/DHAP-autologous SCT
2. Ibrutinib
3. Lenalidomide
4. CAR T-cells
5. Best supportive care

Next steps

- Off study
- R-DHAC x 4 – incomplete response
- Trigeminal nerve distribution numbness and VI nerve palsy with diplopia
- -MRI brain - leptomeningeal infiltrates
- -LP non diagnostic

- → CNS progression

CNS relapse - 2019

Optimal treatment

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1. High dose Mtx
2. Ibrutinib
3. Lenalidomide
4. Allogeneic transplant
5. Best supportive care

Next steps….

- Ritux/Len/Ven x2 – clinical improvement
- CNS response but systemic progression
- H-CVAD x 1 – CMR
- CNS progression – IT methotrexate plus Loxo 305 compassionate access
- Further CNS progression – 26Gy radiotherapy
- Allograft work up…..
- RIP in remission 10 days post RT completion (18m from diagnosis)

Learnings/discussions

- High risk features
- Importance of clinical trials
- Progression can be rapid and aggressive
- BTK inhibitor therapy (and other novel agents) do not necessarily overcome the poor prognostic features in MCL
- Primary refractory disease is bad
- Novel agents can be effective in combination, including in CNS disease
- Lymphoma isn’t the only factor in mortality

Thank you

Questions?