

Lymphoma Treatment Modalities “The Big Picture”

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Disclosures

- None

Learning Objectives

- At the end of this session, participants will be able to:
 - Explain the role of chemotherapy, radiation and bone marrow transplant in the treatment of lymphoma
 - Explain why in some patients with lymphoma the approach is to “watch and wait”
 - Describe how the treatment of lymphoma can affect fertility and list what options can be offered to address this issue

Treatment of Lymphoma

- Type and timing of treatment depends on a number of different factors
 - Lymphoma subtype and tumour behaviour
 - HL versus NHL with their various subtypes
 - Very aggressive versus aggressive versus indolent
 - Presence/absence of mutations
 - Stage
 - Ann Arbor classification I-IV- Limited versus Advanced
 - Presence or absence of “B” symptoms
 - Sites/Organs Involved
 - Patient factors
 - Age, co-morbidities

Chemotherapy

- Backbone of treatment in lymphomas
- Exact “recipe” determined by disease and patient factors
- Monoclonal antibodies are often part of the recipe
 - Rituximab for B-cell NHL (CD 20)
 - Brentuximab for HL (CD 30)

Initiation of Treatment

- Very aggressive and aggressive lymphomas
 - immediate treatment for CR
 - Burkitts, DLBCL, HL
- Limited-stage indolent lymphomas
 - May be considered for involved-field RT
- Advanced-stage indolent lymphomas
 - Decision to treat dependent on symptoms/criteria

Chemotherapy Treatment in Advanced-Stage Indolent NHL

- Local symptoms
- Compromise of normal organ function
- Presence of systemic B symptoms
- Presence of symptomatic extranodal disease
- Cytopenias
- An increase in disease tempo

“Watch and Wait” Strategy

- Patients with advanced- stage indolent lymphoma who don't meet criteria for immediate treatment
- Low disease burden
- No difference in OS or risk of transformation if treatment is delayed in these patients
- Assessed every 3 to 6 months

Radiation Therapy

- Not the primary treatment modality in most patients with lymphoma
 - Exception limited-stage indolent lymphoma
- Is used following short-course chemotherapy (3 or 4 cycles) for limited-stage HL or aggressive NHL
- Is used following chemotherapy treatment for advanced-stage aggressive NHL or HL for consolidation of a residual mass on PET scan

Stem Cell Transplant

- AutoSCT can be used as consolidation treatment in aggressive/very aggressive lymphomas
 - Eligibility and timing dependent on patient and disease factors
- AutoSCT does not have a defined role in indolent lymphomas
- AlloSCT- higher treatment-related mortality

Preservation of Fertility

- Needs to be discussed in detail in at-risk patients
 - Male versus female
 - Patient age- risk of POF increases over age 30
 - Lifestyle factors
 - Disease factors
 - Type of chemotherapy/radiation treatment
- Early referral prior to treatment if possible
 - Amount of time
- Important to document discussions in patient chart
- Psychosocial supports

Fertility Preservation Options

- Sperm cryopreservation for males
- Oocyte or embryo cryopreservation for females
- Other experimental treatments
- Radiation Shielding
- Ovarian transposition (females)

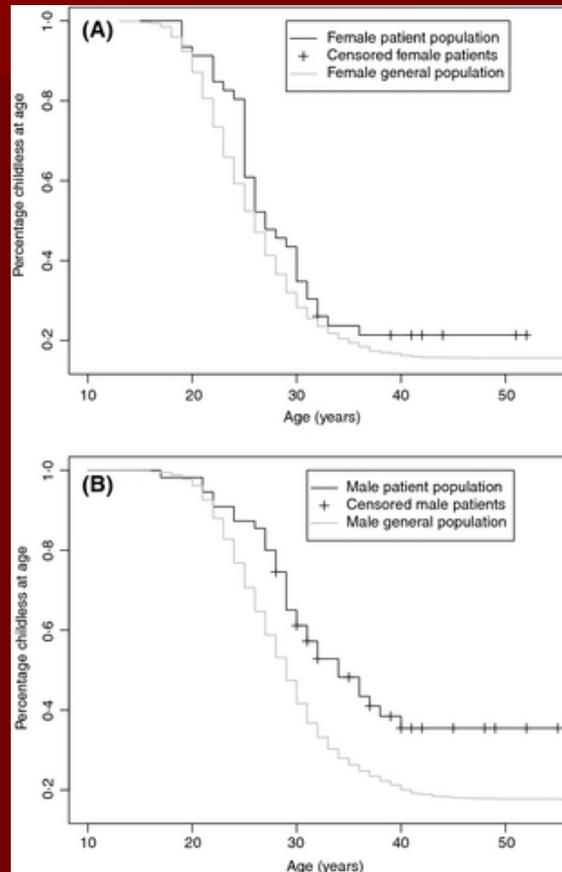
What about Gonadotropin Releasing Hormone Agonists?

- GNRH agonists did not influence the rate of premature ovarian failure when given to female lymphoma patients
- Therefore, despite the theoretical advantage of a pharmacologic option to suppress ovarian function, it did not work in long-term followup!
 - (Demeestere et al., 2016)

Lymphoma Patients At-risk for Infertility

- HL- little or no risk of premature ovarian failure with ABVD(Kaaij et al., 2012)
 - Risk 3 percent- patients less than 32 y.o.
 - Risk 9 percent- patients greater than 32 y.o.
 - Also low risk of permanent male sterility
- Indolent NHL
 - R-bendamustine risk unknown
- Aggressive NHL
 - RCHOP

Parenthood in long-term survivors after CHOP with or without etoposide treatment for aggressive lymphoma (Meissner et al., 2014)



However...

- Those low risks for infertility will only hold if patient achieves a CR with these treatments
- Risk increases dramatically if patient requires salvage chemotherapy and/or ASCT
- Discussions need to be individualized
- Recommended to wait for 2 years following completion of cytotoxic chemotherapy before trying to conceive

Conclusions

- Chemotherapy is the backbone of treatment
- Radiation therapy and ASCT have a role
- “Watch and wait” can be considered for asymptomatic patients with advanced-stage indolent lymphomas with low tumour burden
- Low risk of infertility with chemotherapy regimens for aggressive lymphoma but increases with salvage treatments
- Fertility preservation options exist but GnRH agonists are not effective

References

- Demeestere, I., Brice, P., Peccatori, F. A., Kentos, A., Dupuis, J., Zachee, P., ... Englert, Y. (2016). No Evidence for the Benefit of Gonadotropin-Releasing Hormone Agonist in Preserving Ovarian Function and Fertility in Lymphoma Survivors Treated With Chemotherapy: Final Long-Term Report of a Prospective Randomized Trial. *Journal of Clinical Oncology*, *34*(22), 2568–2574. <http://doi.org/10.1200/JCO.2015.65.8864>
- Kaaij, M. A. E. van der, Heutte, N., Meijnders, P., Abeilard-Lemoisson, E., Spina, M., Moser, E. C., ... Kluin-Nelemans, H. C. (2012). Premature Ovarian Failure and Fertility in Long-Term Survivors of Hodgkin's Lymphoma: A European Organisation for Research and Treatment of Cancer Lymphoma Group and Groupe d'Étude des Lymphomes de l'Adulte Cohort Study. *Journal of Clinical Oncology*, *30*(3), 291–299. <http://doi.org/10.1200/JCO.2011.37.1989>
- Meissner, J., Tichy, D., Dietrich, S., Schmitt, T., Ziepert, M., Kuhnt, E., ... Ho, A. D. (2014). Parenthood in long-term survivors after CHOP with or without etoposide treatment for aggressive lymphoma. *British Journal of Haematology*, *166*(4), 612–615. <http://doi.org/10.1111/bjh.12877>