How to treat transformed lymphoma

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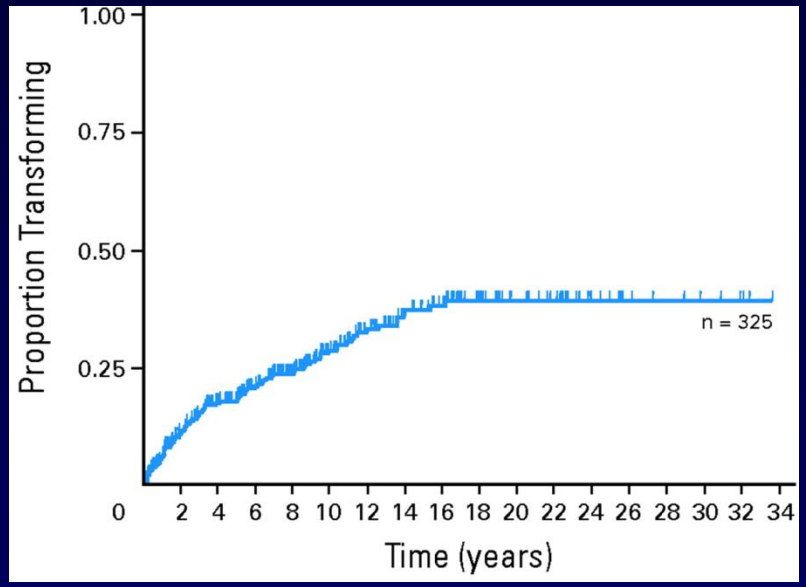
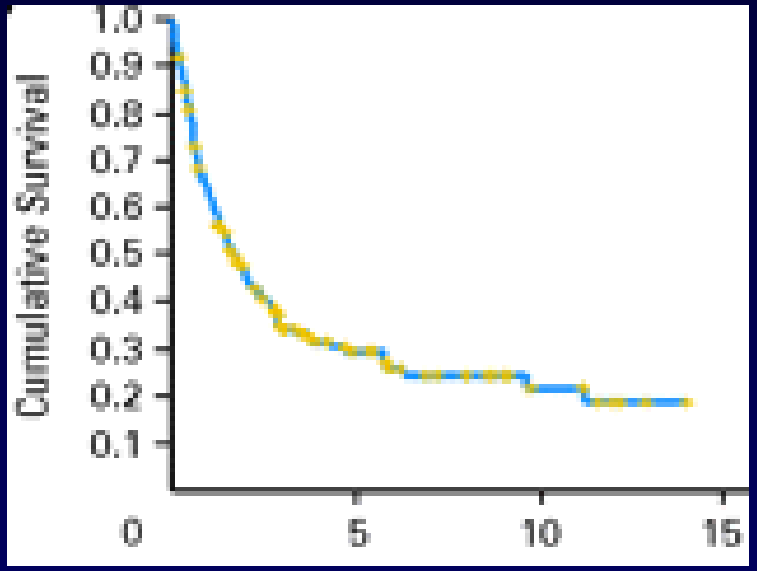
The past:
Incidence and Outcome of Transformed NHL





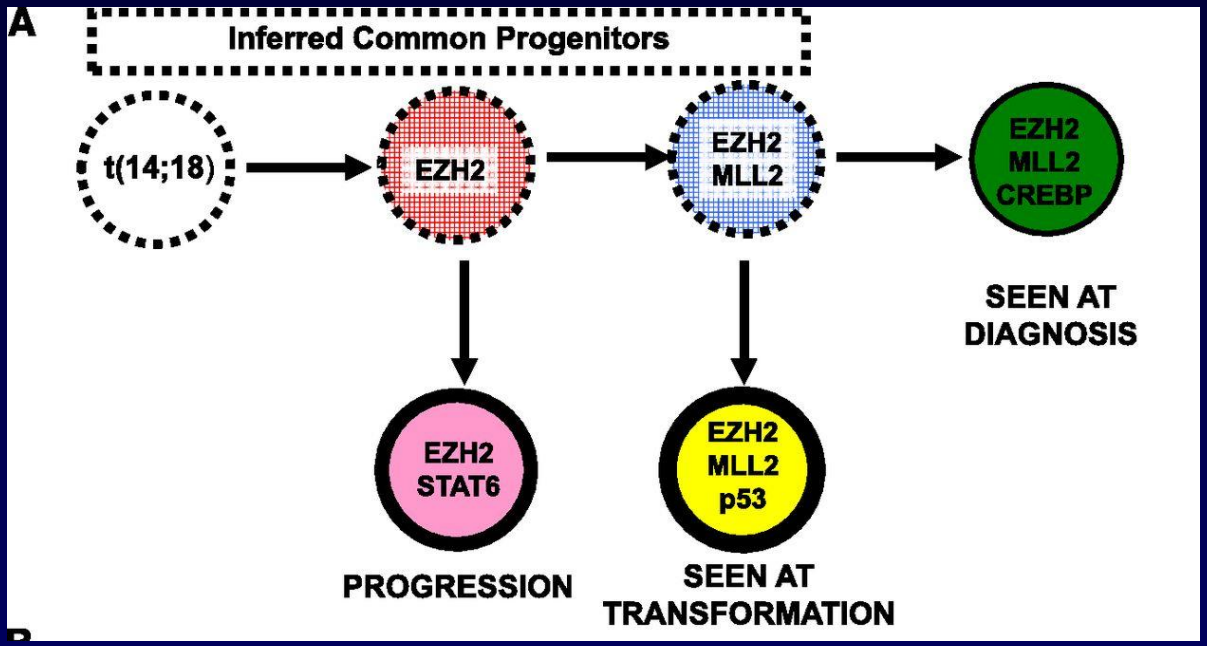
Steady risk of 3% per year for first 15 years of diagnosis
Treatment (or lack thereof) does not impact risk
Poor overall survival, particularly for advanced stage disease

Montoto et al, *JCO* 25: 2426
Al-Tourah et al, *JCO* 26: 5165

Key recent themes in transformed FL

- Remains an important cause of morbidity and mortality for patients with FL.
- Increased biological understanding will impact future clinical options
  - Heterogeneity of mutations have differential outcomes, i.e. “double hit” GCB DLBCL.
- Incidence of HT may be decreasing in rituximab era.
- Outcomes have improved significantly, for unclear reasons.
- These improved outcomes have led to significant OS improvements in FL.

New biologic understanding of transformed FL

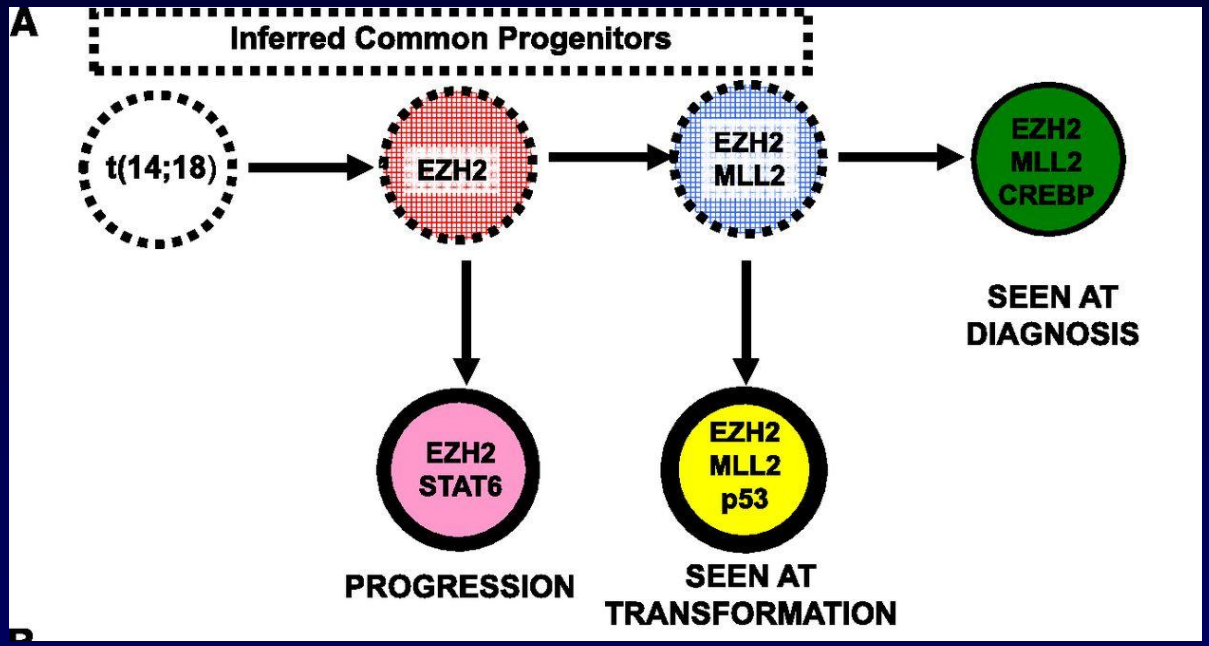


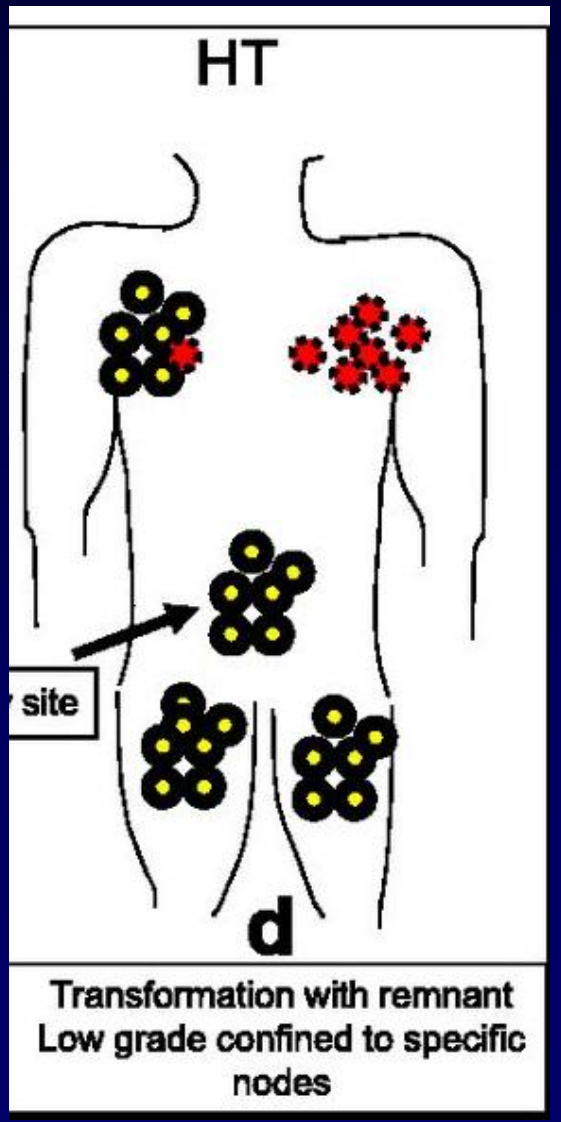
Numerous subclones present in FL.

Population that arises at HT is not directly descended from diagnosis or relapsed population.

Casulo, Burack, Friedberg *Blood* 125: 40-7

New biologic understanding of transformed FL



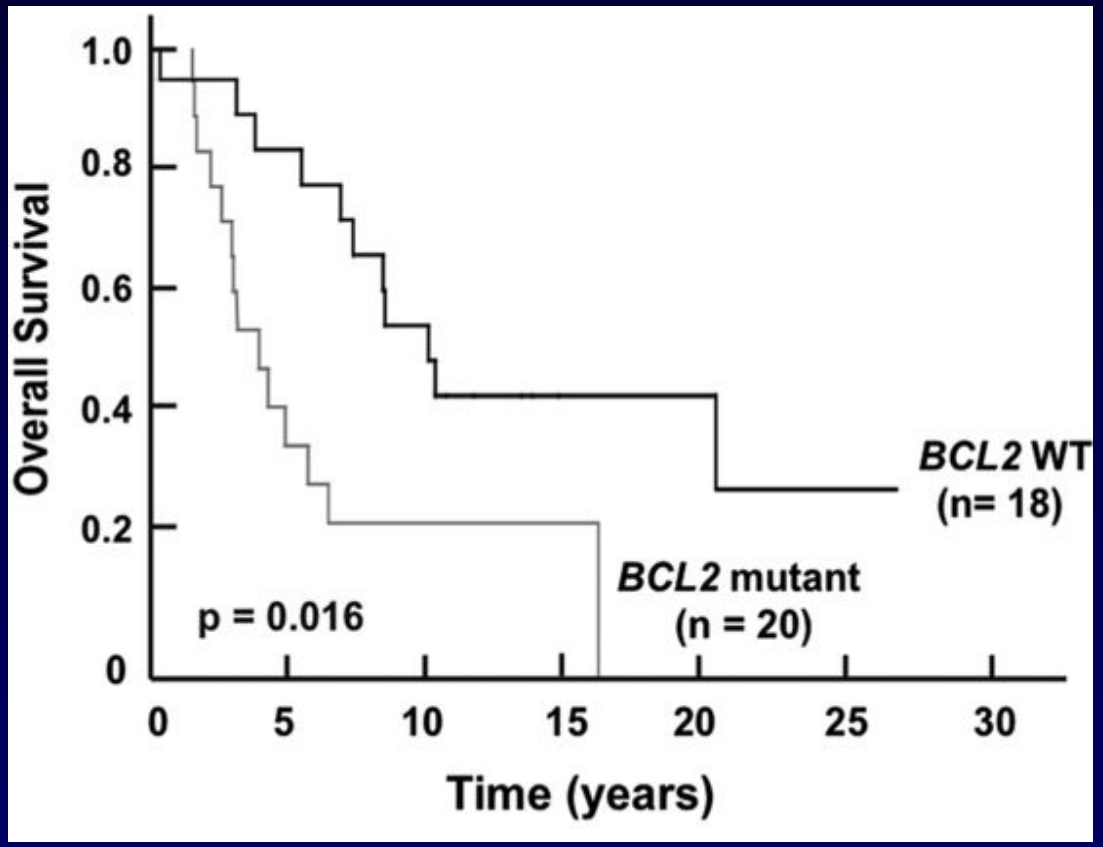


Casulo, Burack, Friedberg *Blood* 125: 40-7

BCL-2 mutations and OS in FL
Increased HT risk with mutations

Bcl-2 mutation:
- Decreased OS
- Transformation risk

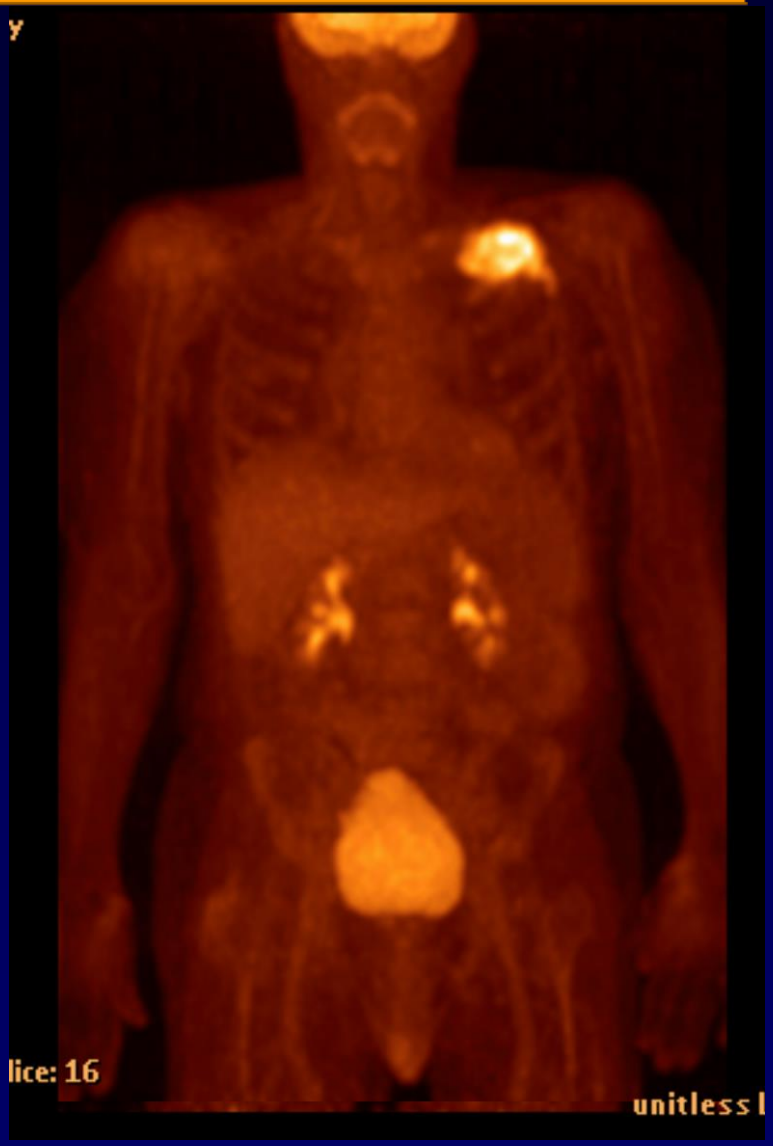
However….
- Pre-rituximab era
- Poor OS in controls
- Median OS 10 yrs.



Correia et al, *Blood* in press 2015

FDG-PET in transformed FL

- N=33 patients
  - SUV of the biopsy site ranged from 3-38, mean 14, median 12.
  - majority of transformations have a high SUV max for pretreatment staging study.

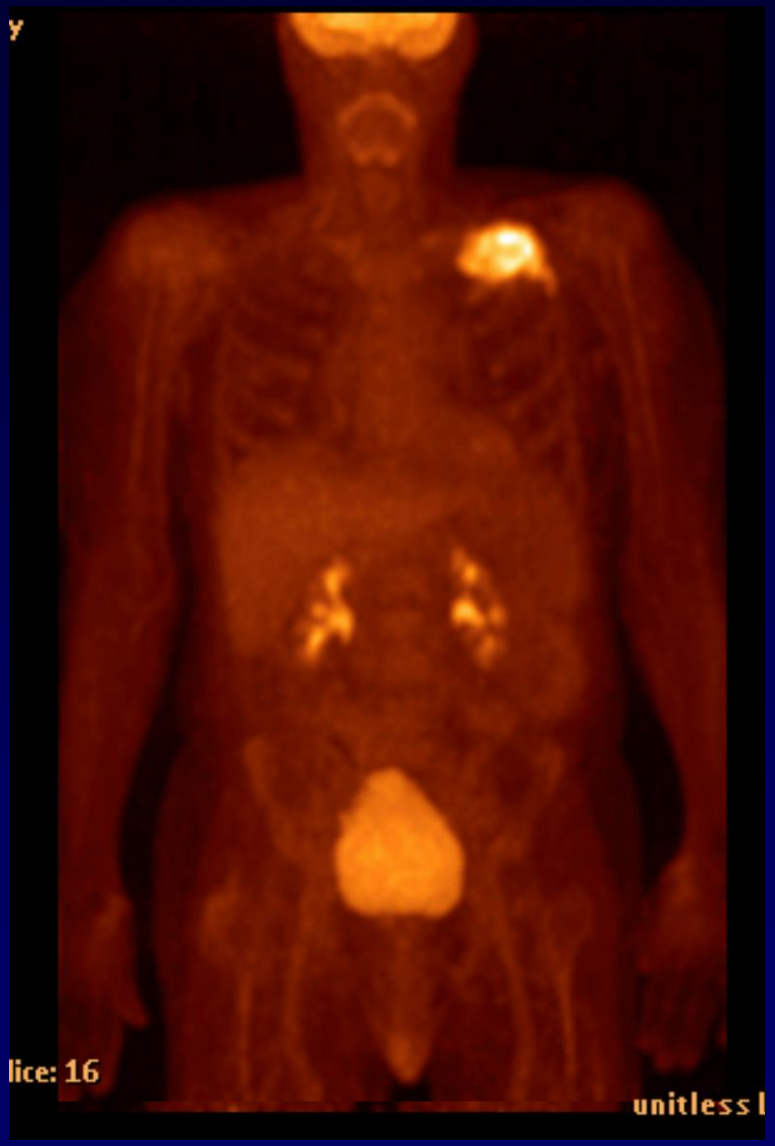


Noy et al, *Annals Oncol 20:508*

FDG-PET in transformed FL

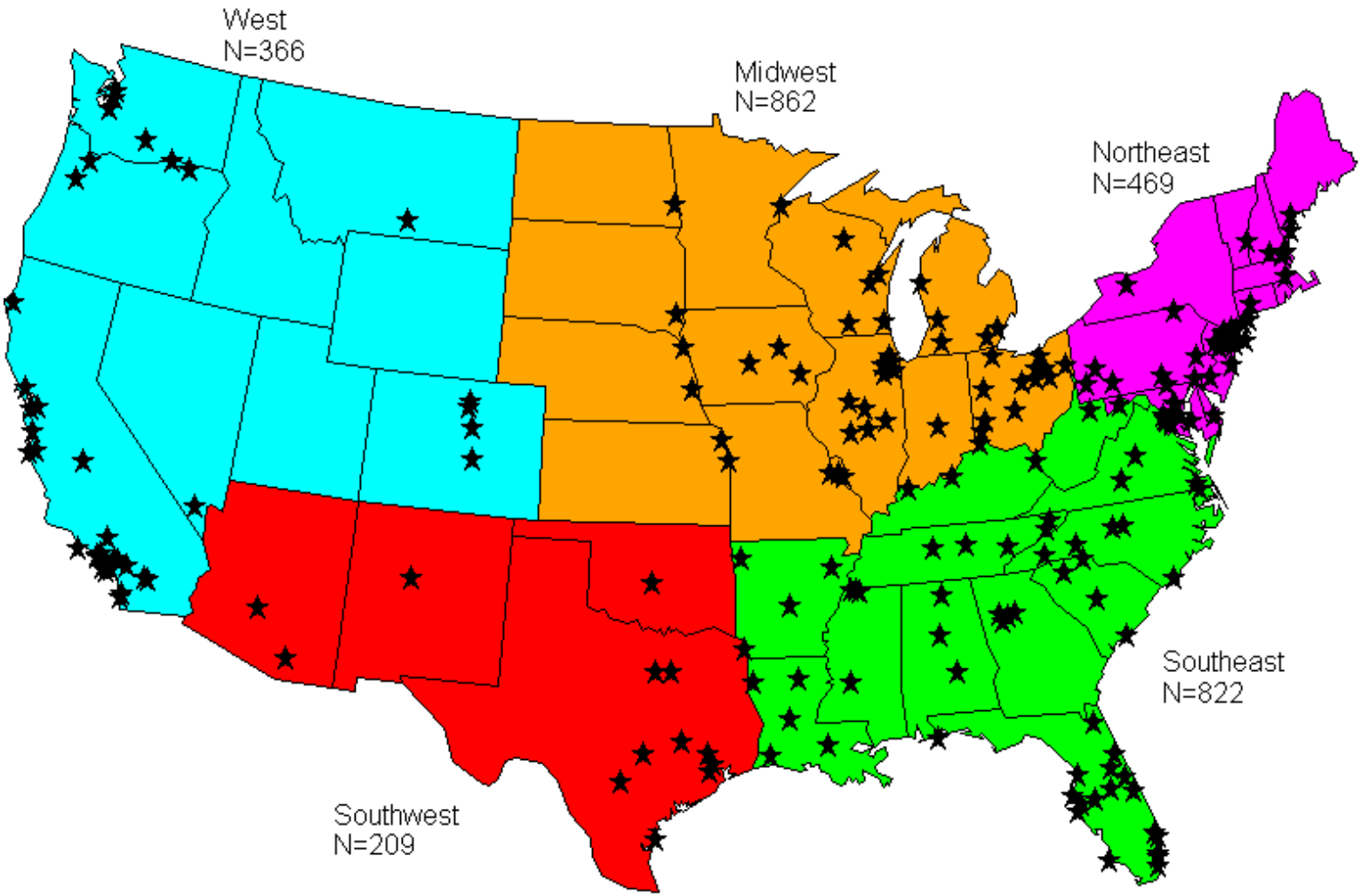
- N=33 patients
  - SUV of the biopsy site ranged from 3-38, mean 14, median 12.
  - majority of transformations have a high SUV max for pretreatment staging study.

PET important tool to select biopsy site in suspected HT



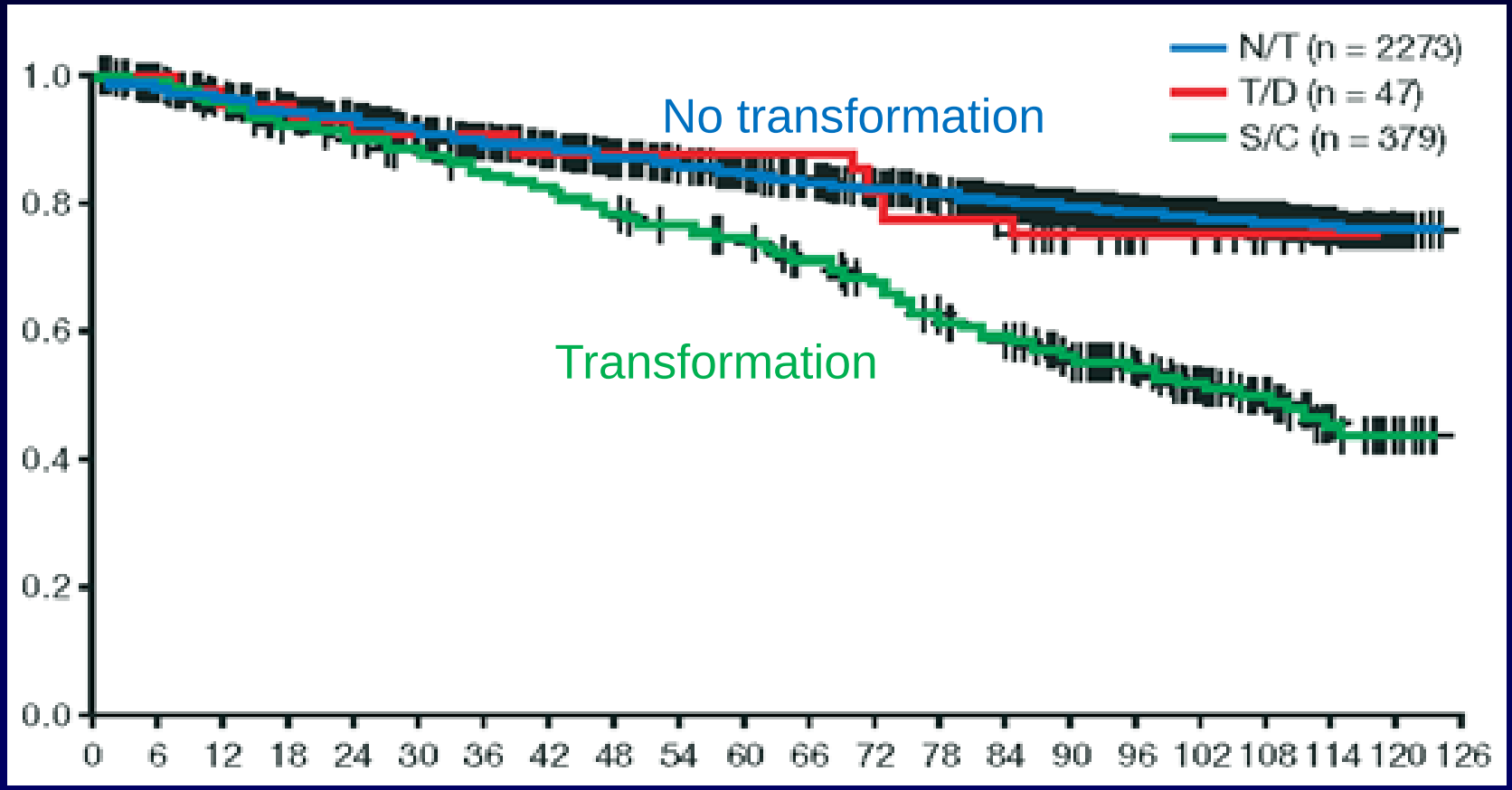
Noy et al, *Annals Oncol 20:508*

National LymphoCare Study: 2004 - 2007



N = 2728

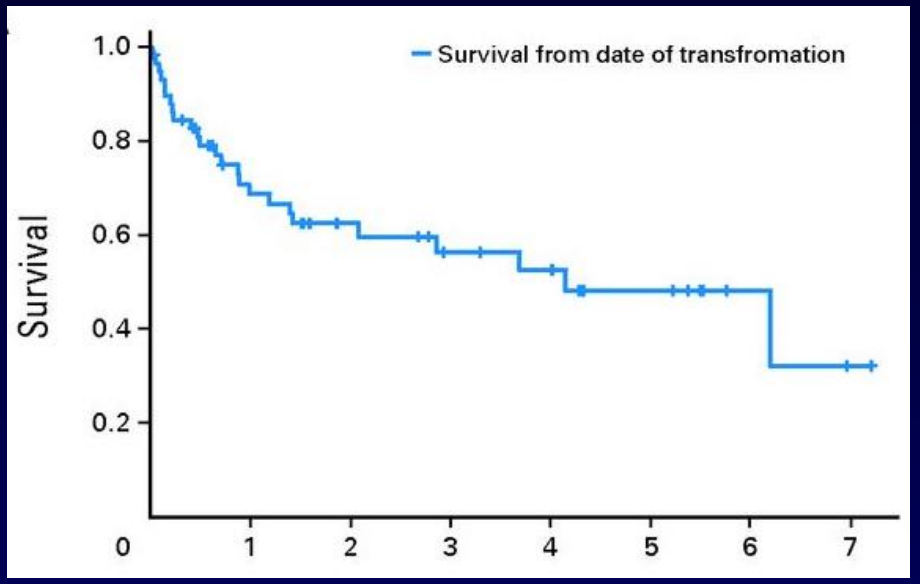
OS from FL diagnosis: LymphoCare data

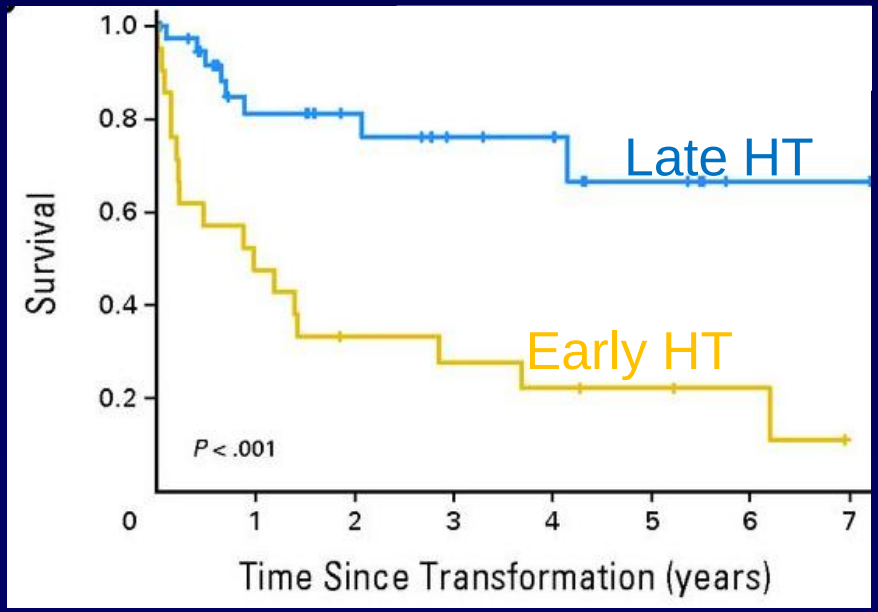


Unpublished data, NLCS

Outcome (OS) of HT has improved

- N= 631 FL patients SPORE
  - 60 patients developed HT, 51 biopsy proven.
- Estimated HT rate of 2%/yr.
  - Median f/u 5 yrs.
- Median OS post HT 50 months
  - Superior in pts > 18 months after FL diagnosis compared with patients with earlier HT (P < .001).

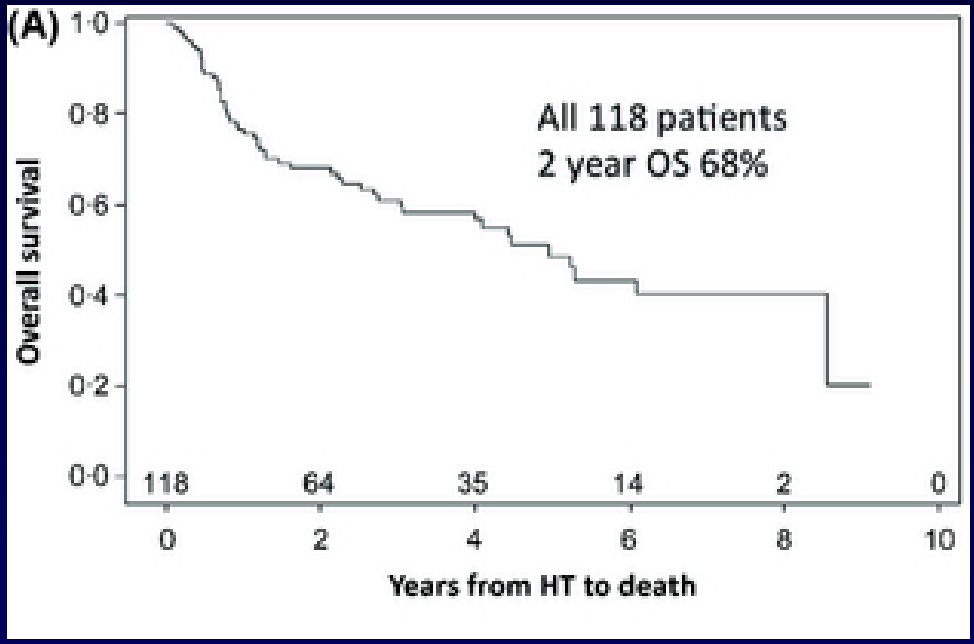




Link et al, *JCO* 31:3272

Outcome (OS) of HT has improved

- NCCN database, N=118:
  - biopsy confirmed HT
  - Survival improved with no prior FL therapy



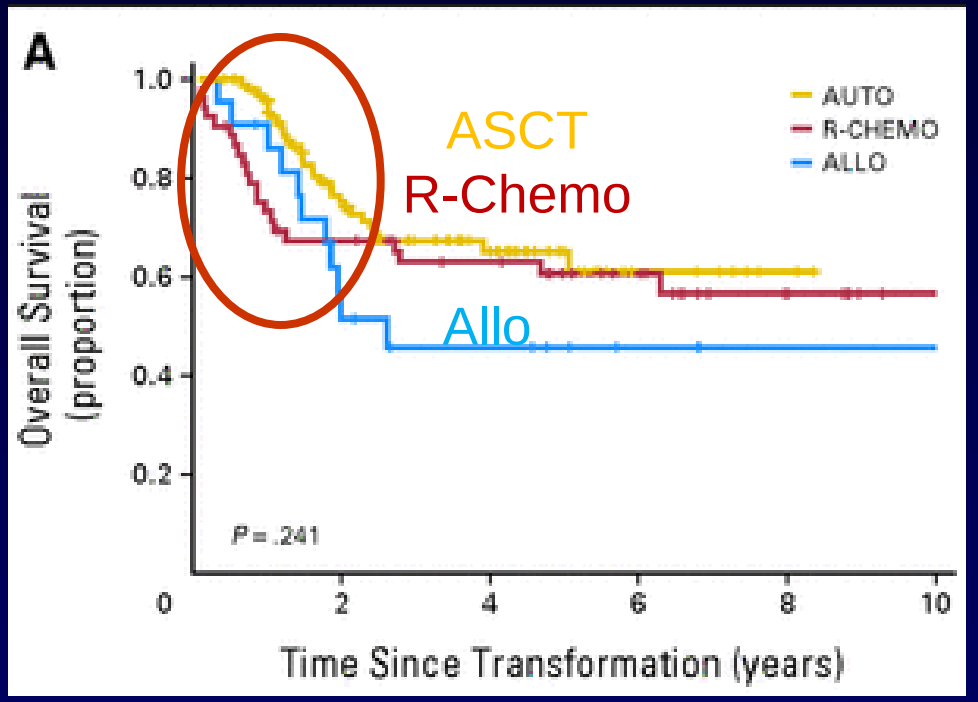
Ban Hoefen…Friedberg, *BJHaem* 163: 487

HT Data considerations

- No randomized or prospective trials
- Differential definitions
  - Clinical vs. pathological confirmation
  - Composite NHL vs. transformation
- Patient selection
  - Single institutional vs. registry
  - Elderly under-reported
- Rituximab era vs. no rituximab

Role of ASCT for HT

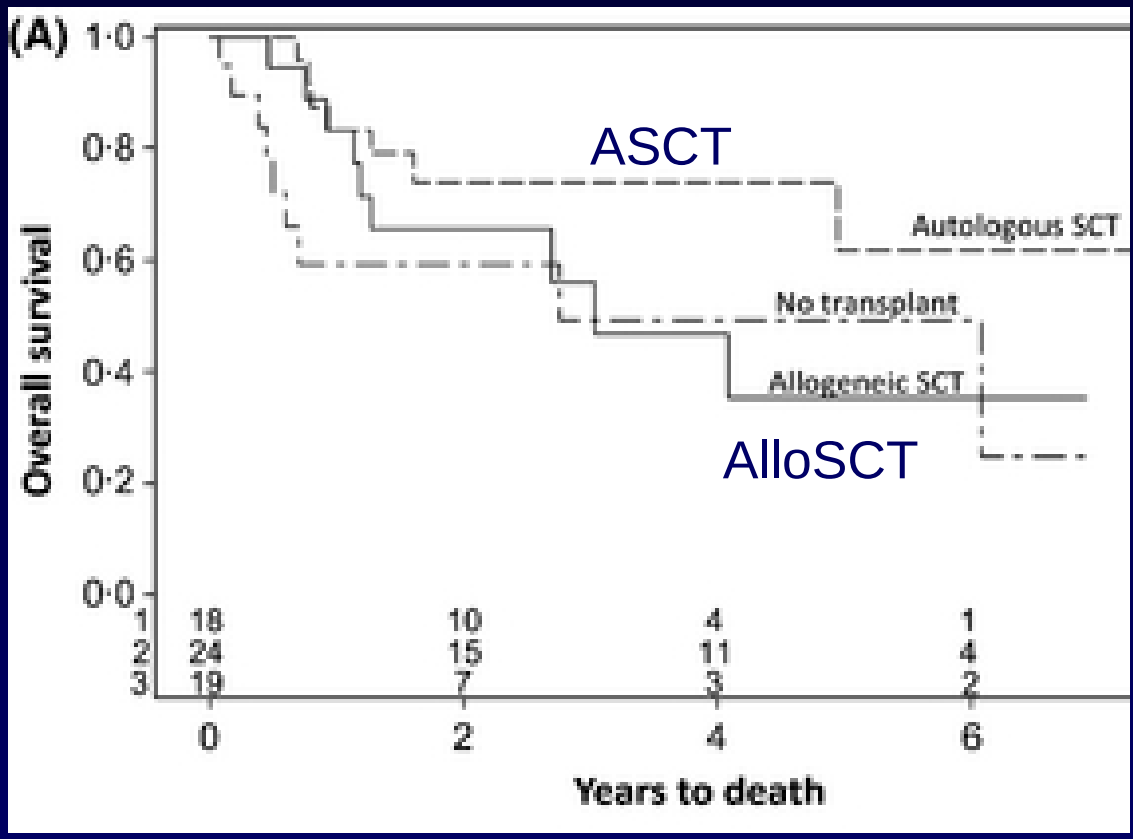
- N=172 Canadian Registry
  - 22 (13%) alloSCT
  - 97 (56%) ASCT
  - 53 (31%) R-Chemo
- ASCT had improved OS compared with R-Chemo alone (*P* = .12).
  - OS and PFS similar between those treated with ASCT and alloSCT.



Villa et al, *JCO* 31: 1164

Role of ASCT for HT

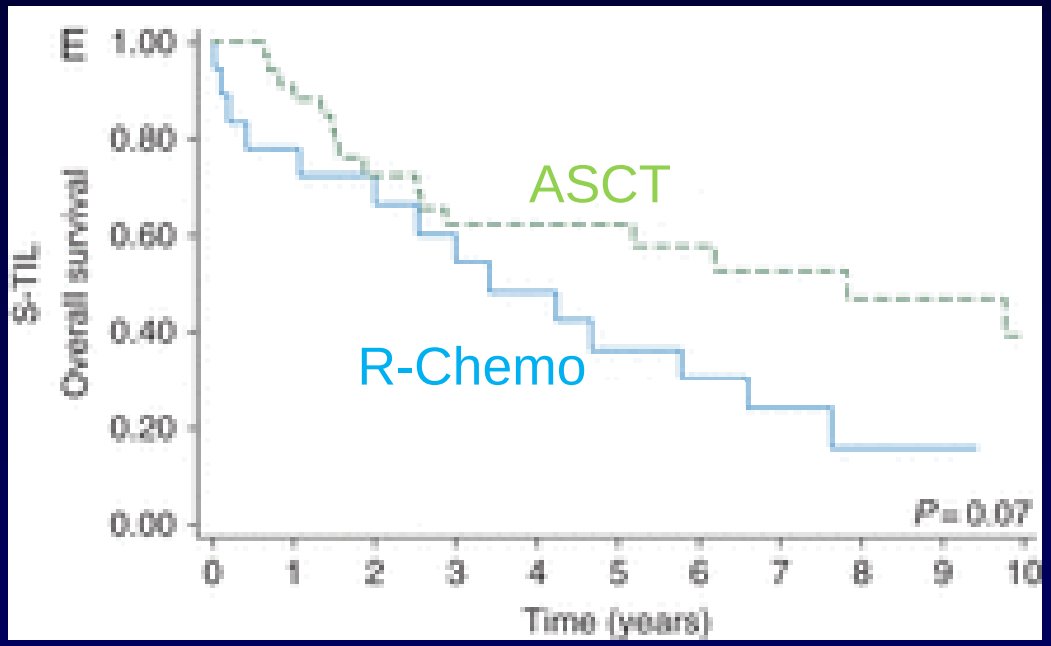
- NCCN database:
  - ASCT ≤60 years (*n* = 24), 2-year OS was 74%.
  - For non-transplanted aged ≤60 years (*n* = 19), the 2-year OS was 59%.



Ban Hoefen et al, *BJHaem* 163:487

Role of ASCT in HT

- N=85 pts from Denmark:
  - OS improved with ASCT for “sequential” rather than “composite” HT.
  - Median f/u 3.4 yrs.
  - Similar findings to other studies.



Madsen et al, *Annal Oncol* 26:393

Conclusions: ASCT for HT in rituximab era

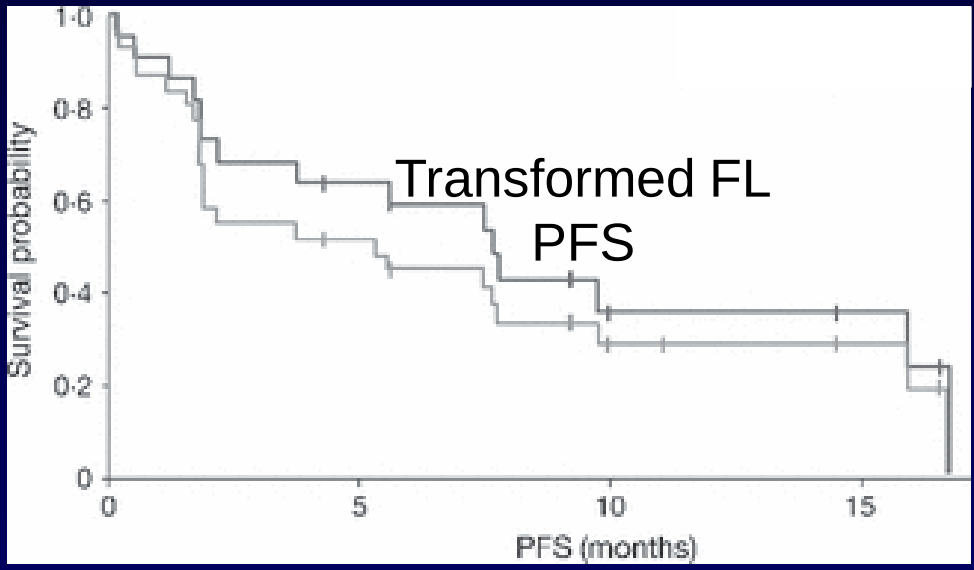
- Outcomes in younger patients relatively favorable, with or without ASCT.
- Nonrandomized studies suggest small benefit of ASCT, with relatively short follow-up.
- No clear role for alloSCT.
- No evaluation of rituximab maintenance.

Conclusions: ASCT for HT in rituximab era

- Outcomes in younger patients relatively favorable, with or without ASCT.
- Nonrandomized studies suggest small benefit of ASCT, with relatively short follow-up.
- No clear role for alloSCT.
- Most patients older or frail and not ASCT candidates

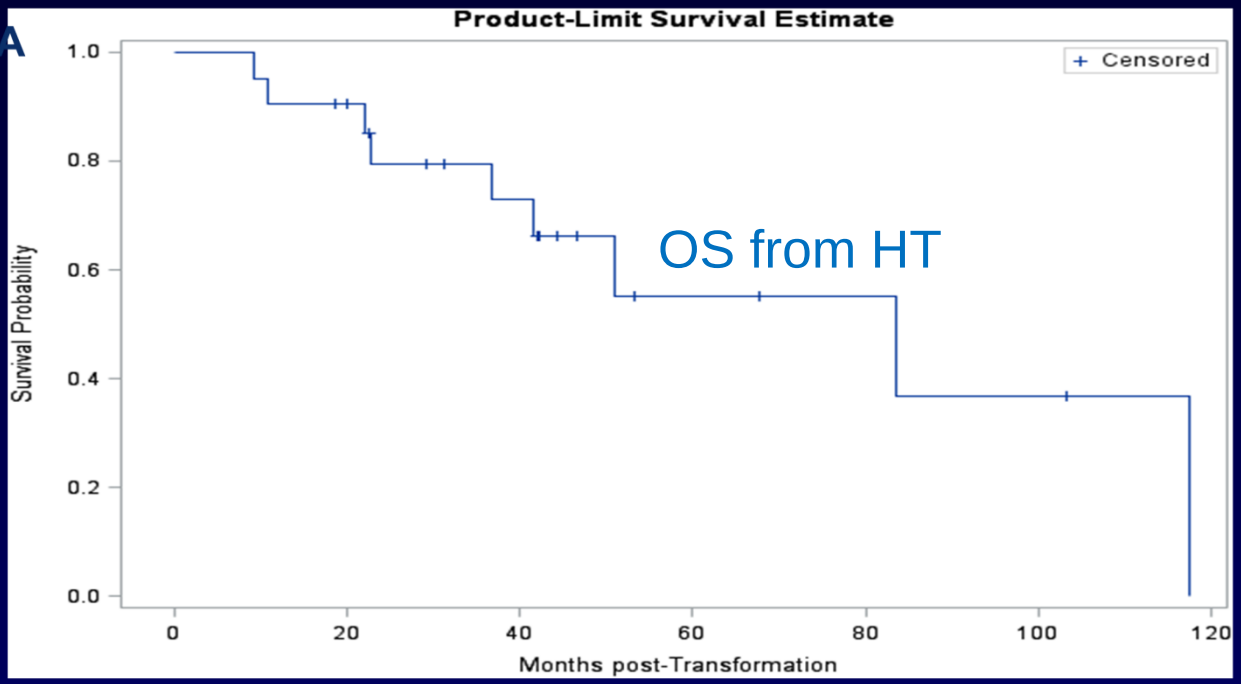
Lenalidomide for HT

- N=33 pts
  - 25 mg dose
  - ORR 57%
  - Median DOR 1 yr
  - FL > other histologies



Czuczman et al, *BJHaem* 154: 477

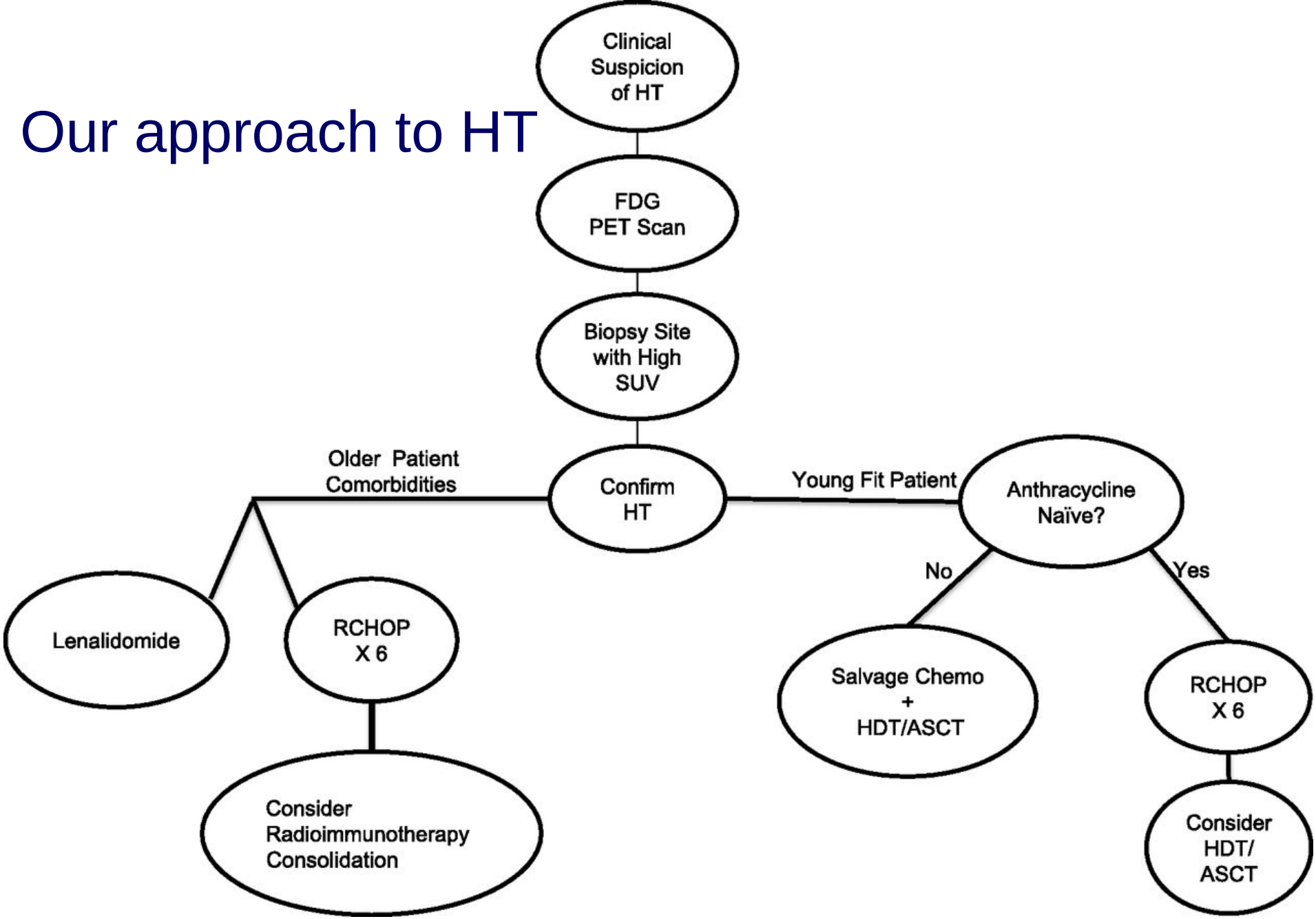
Consolidative RIT for HT: *Patients unfit for ASCT*



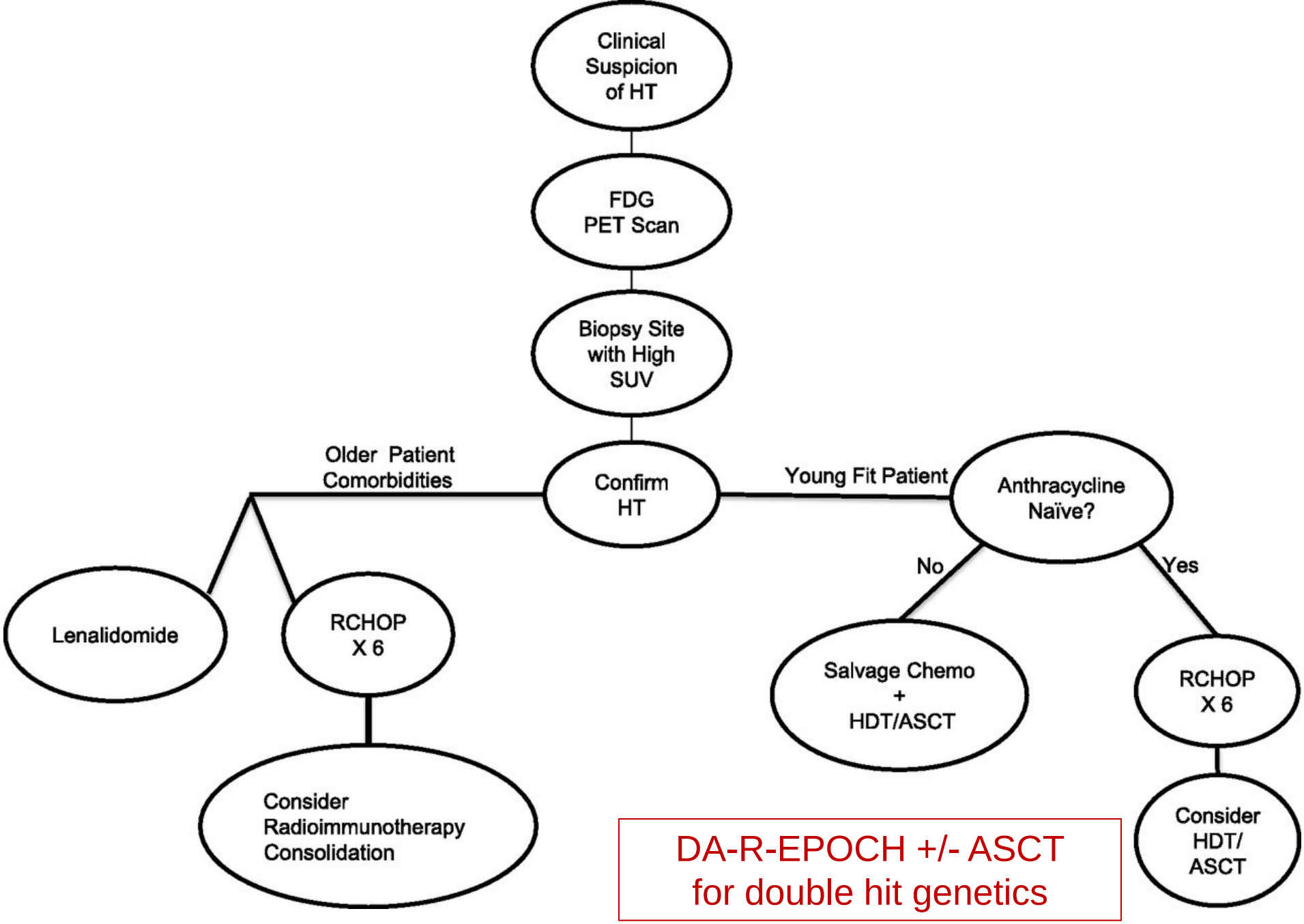
- N=21; R-CHOP + tositumomab or ibritumomab
- Median OS from HT: 84 months
- 2 cases of MDS/AML

Reagan et al, *ASH* 2014

Our approach to HT



Casulo, Burack, Friedberg *Blood* 125: 40, 2015


Clinical Suspicion of HT
FDG PET Scan
Biopsy Site with High SUV
Confirm HT
Older Patient Comorbidities
Young Fit Patient
Lenalidomide
RCHOP X 6
Consider Radioimmunotherapy Consolidation
Anthracycline Naïve?
No
Yes
Salvage Chemo + HDT/ASCT
RCHOP X 6
Consider HDT/ ASCT
DA-R-EPOCH +/- ASCT for double hit genetics

Potentially rational agents for HT

- ABT-199
- Alisertib
- Immune-based approaches, including checkpoint inhibition

Thank you!
Questions?