UCSF Helen Diller Family Comprehensive Cancer Center

Understanding the Role of Autologous Transplant and Consolidation Strategies: Opinions and Options

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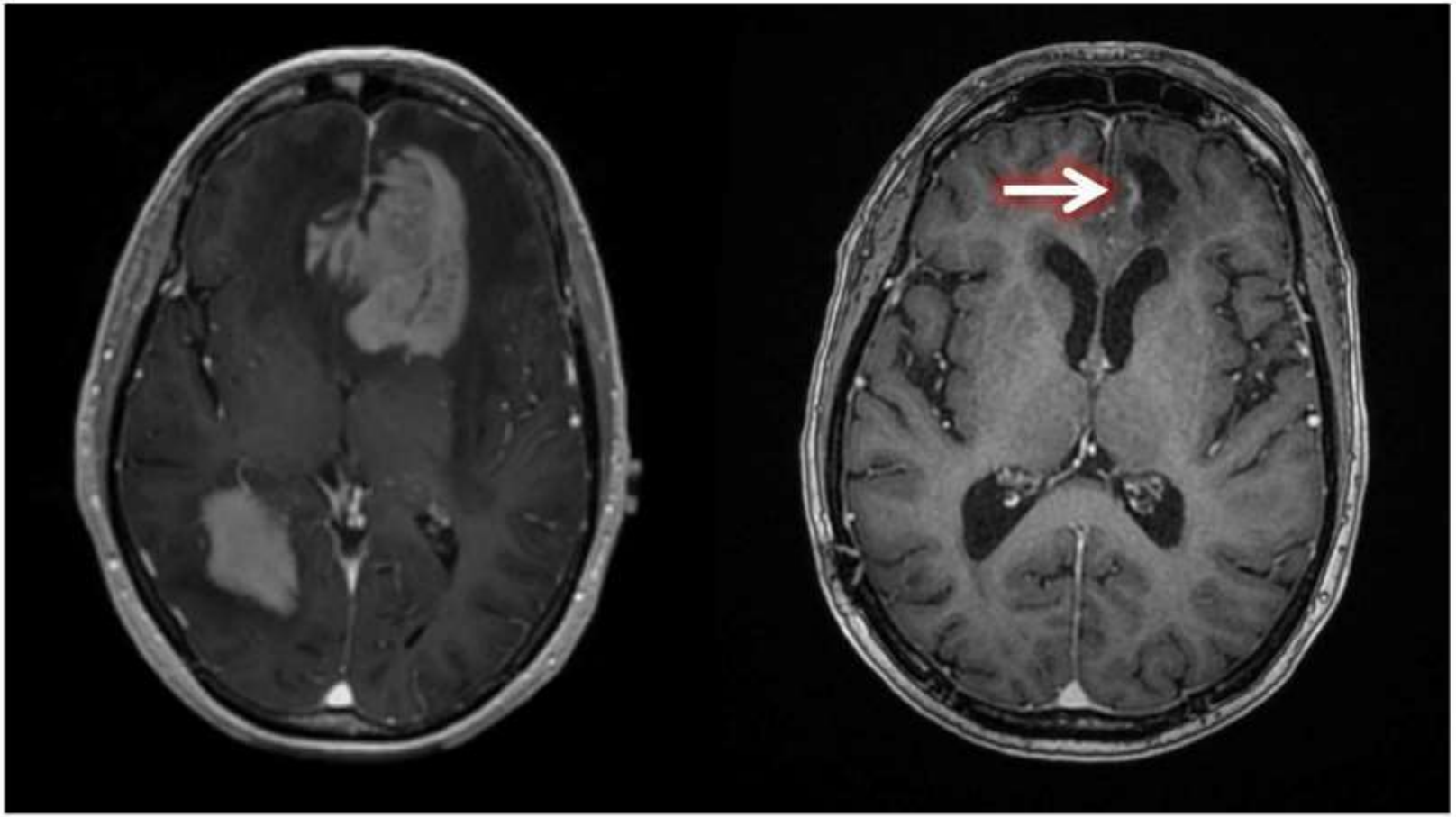
Presented By James Rubenstein at 2019 ASCO Annual Meeting

- I receive research support from Celgene and Genentech
- I will discuss investigational uses of lenalidomide, pomalidomide.

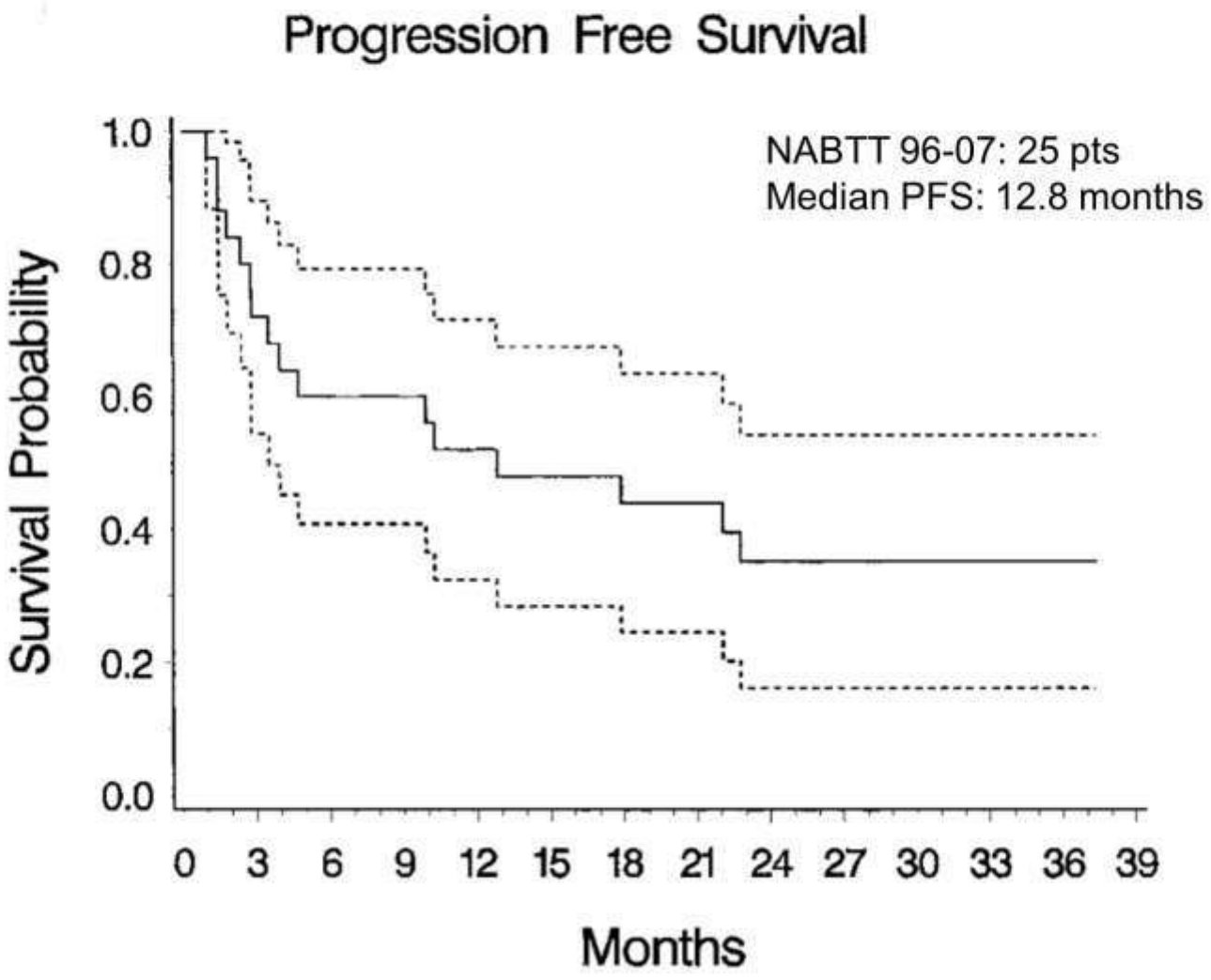
Primary CNS Lymphoma: Response to Induction



At Diagnosis

After MT-R Induction

High Dose-MTX Monotherapy in PCNSL



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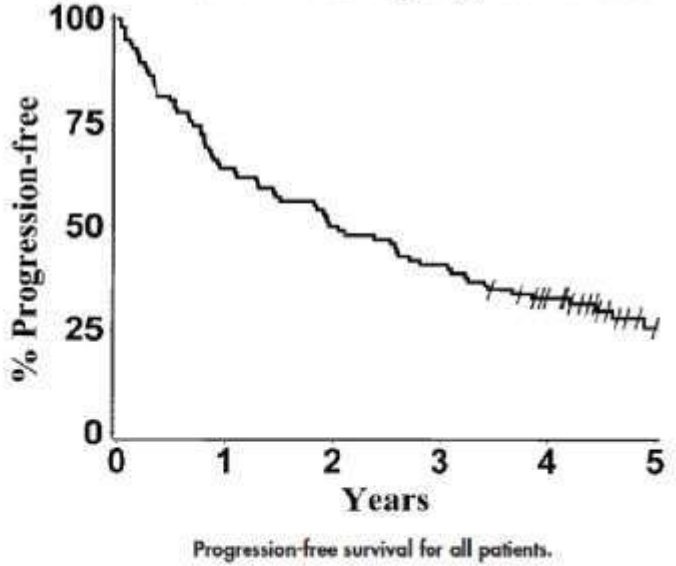
Consolidation Strategies in PCNSL

- Whole Brain Radiotherapy
  - Standard Dose
  - Reduced Dose
- High-Dose Chemotherapy
  - Myeloablative (ASCT)
  - Non-Myeloablative

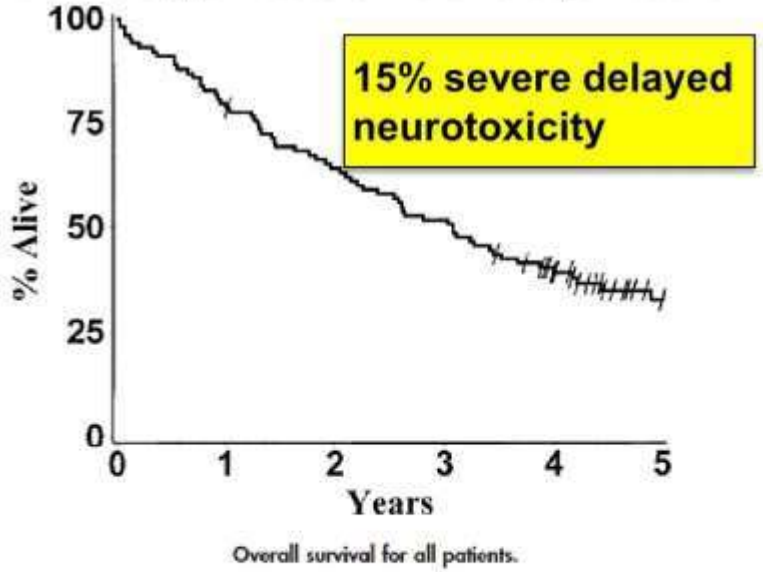
Combined Modality Therapy: RTOG 9310

- HD-MTX + IT-MTX
- Procarbazine
- Vincristine
- WBRT Consolidation

Median OS age ≥ 60: 21.8 months vs. age <60: 50.4 months *p<0.001*



Progression-free survival for all patients.

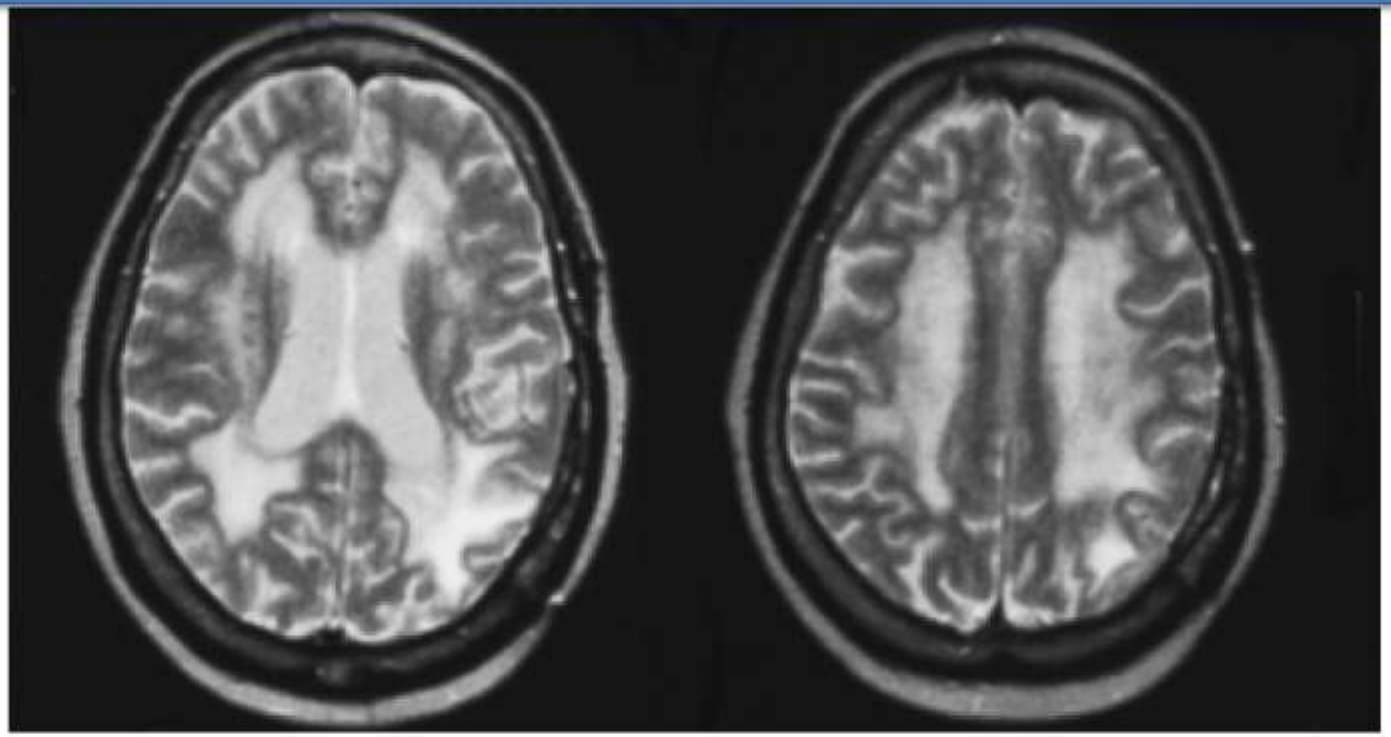


Overall survival for all patients.

Median PFS = 24 months
102 patients

DeAngelis et al., J Clin Oncol 2002

WBXRT Toxicity



Encephalopathy: Memory Deficits, Apathy, Decreased Concentration, Urinary Incontinence and Gait Disturbance

High Dose Chemotherapy Strategies in PCNSL

- Cytoxan/BCNU/VP16 (CBV)
- BCNU/VP16/Ara-C/Melphalan (BEAM)
- Thiotepa/Busulfan/Cytoxan (TBC)
- BCNU/Thiotepa

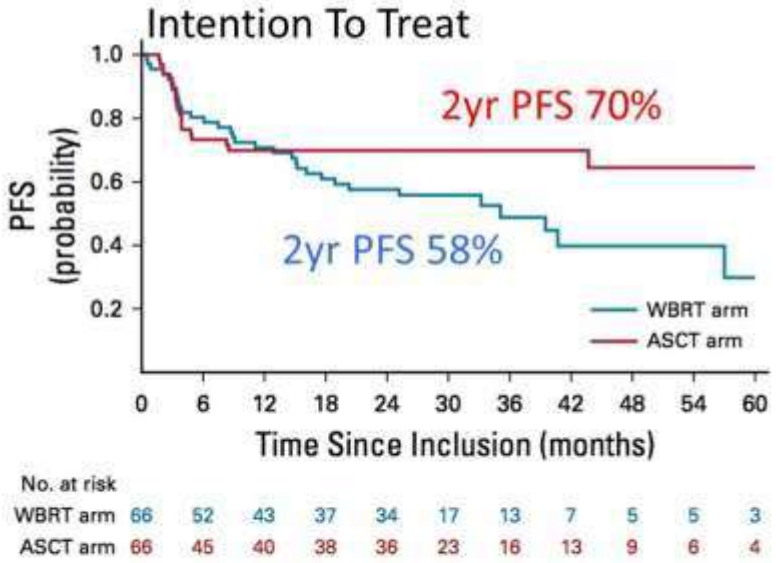
- VP16/Ara-C (EA) **Non-Myeloablative**

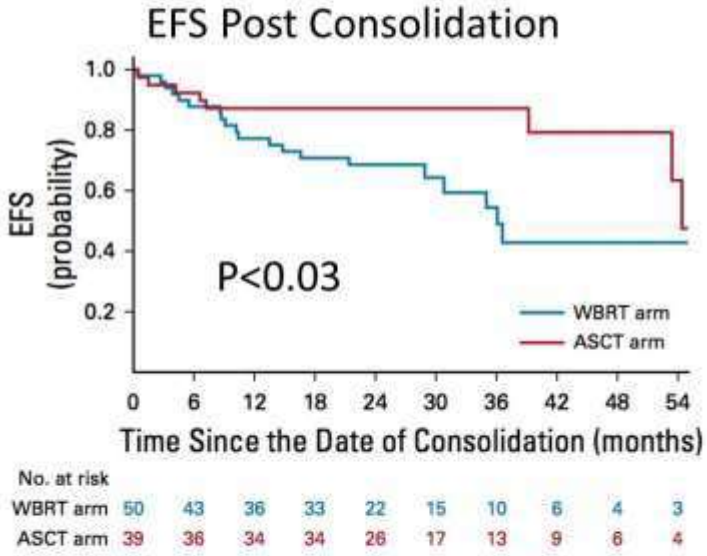
Randomized Control Trials Comparing WBXRT vs. ASCT as Consolidation in PCNSL

Study	PRECIS	IELSG 32
Centers	France	Italy, Germany, UK, Switzerland
Eligibility	Age ≤60	Age ≤65
WBRT	40 Gy	36 Gy if ≥SD; 40 Gy if PD
Preparative Regimen	Thiotepa, Busulfan, Cy	BCNU/Thiotepa

PRECIS: Randomized Phase II: WBRT vs. ASCT

140 pts, median age 55
Induction: R-MBVP Induction (rituximab/MTX/BCNU/Prednisone)
Consolidation independent of response: TBC Preparative regimen vs. 40 Gy WBXRT
Primary Endpoint: 2-yr PFS





Median Follow-up 33.5 months
Houillier et al. J. Clinical Oncology 2019

11% TRM with TBC

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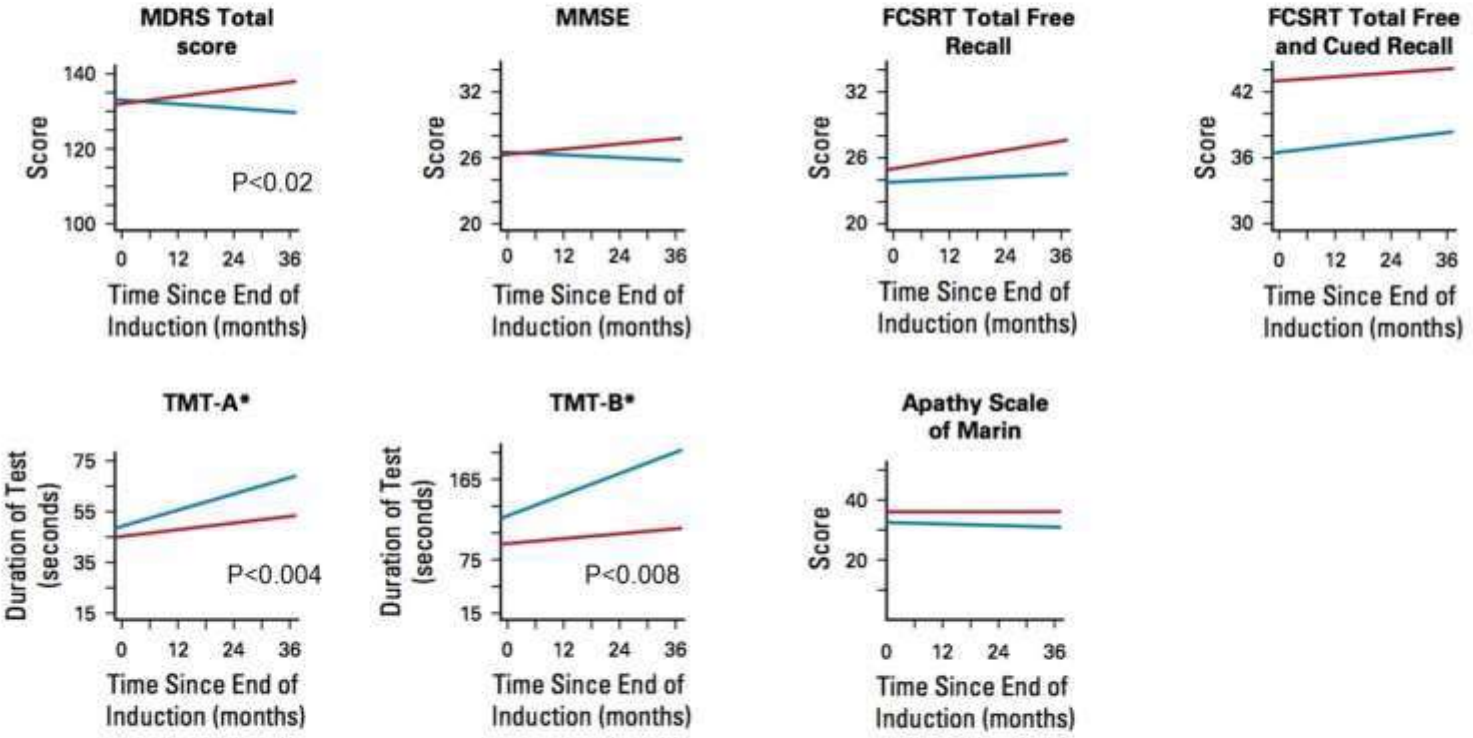
PRECIS: Exploratory Neurocognitive Analysis

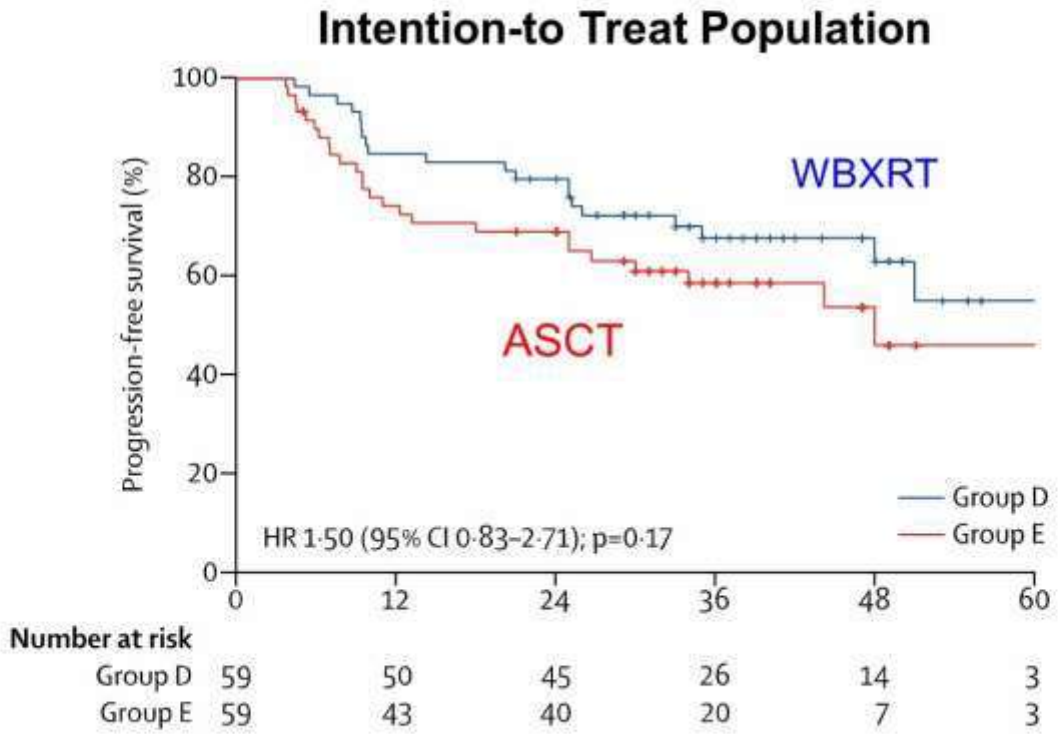


After WBXRT > 50% pts-> decline in test scores
After ASCT >50% pts->improvement in test scores

ASCT=red
WBRT=blue

Conclusions of IELSG32 Second Randomization

122 pts median age 58: eligible for second randomization:
227 pts enrolled Induction: MATRix vs. MTX + Ara-C vs. R-MTX + Ara-C
Consolidation – CR, PR or SD: BCNU/TT Preparative regimen vs. 36 Gy (+ 9 GY boost) WBXRT
Primary Endpoint: 2-yr PFS



No difference in 2 yrs PFS

Median Follow-up 40 months
Ferreri at al., Lancet Haematology 2017

3.4% TRM with ASCT but 5 late deaths

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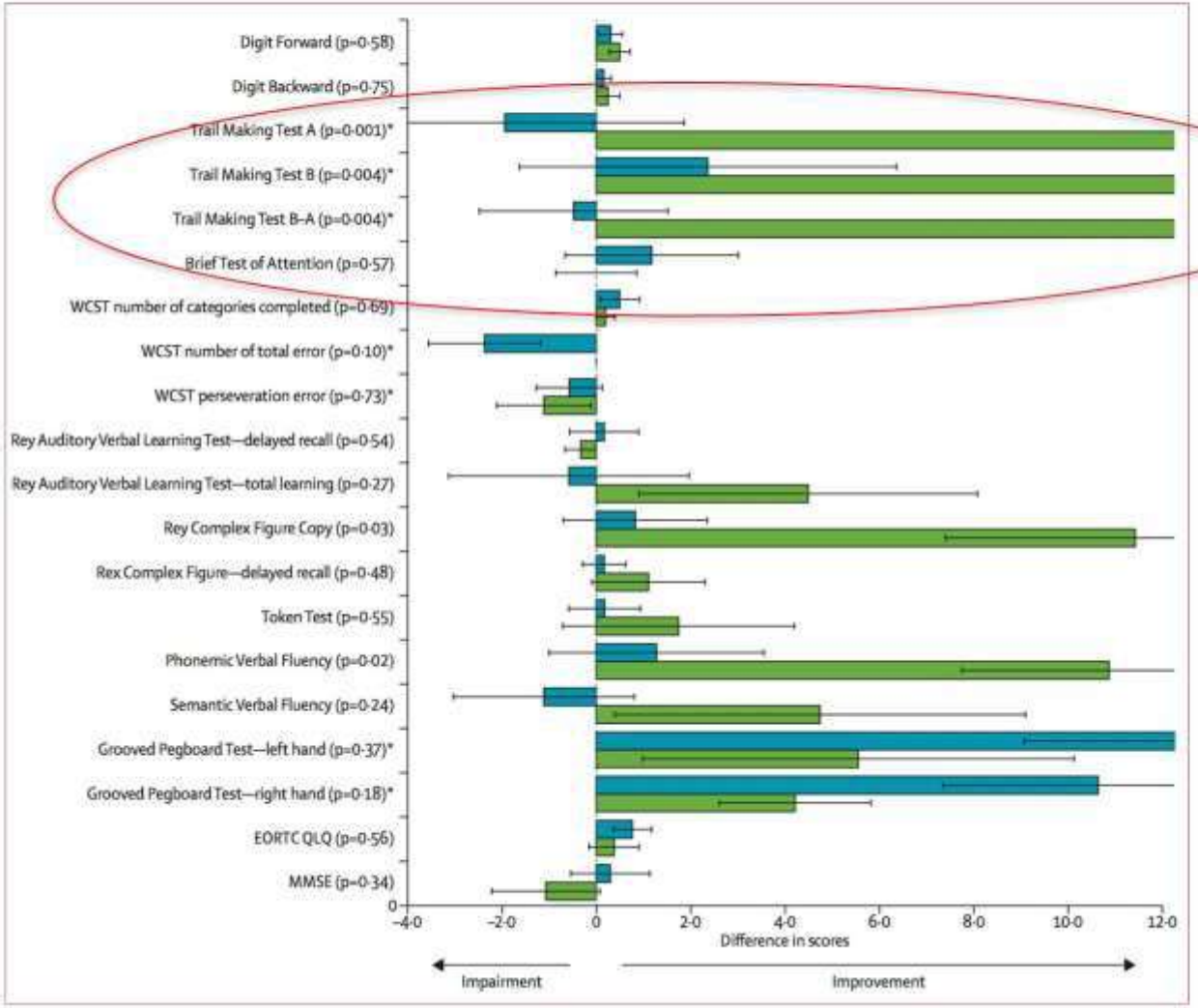
IELSG-32 Neurocognitive Analysis



ASCT
WBXRT

At 2 yrs, pts treated w/ WBXRT: **declines** in executive function & learning

At 2 yrs, pts treated w/ ASCT: **improvements** in executive function, memory & QOL

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