AJCC-Staging for Retinoblastoma: One System Predicts Both Globe Salvage and Patient Mortality

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Authors – American Joint Committee on Cancer Ophthalmic Oncology Task Force (AJCC-OOTF)

1. Paul T. Finger, MD – USA
2. Ankit Singh Tomar, MD - India
3. Brenda Gallie, MD- Canada
4. Ashwin Mallipatna, MBBS, MS- Canada
5. Tero T. Kivelä, MD - Finland
6. Chengyue Zhang, MD - China
7. Junyang Zhao, MD - China
8. Matthew W. Wilson, MD - USA
9. Rachel C. Brenna, MD - USA
10. Michala Burges, BS - USA
11. Jonathan Kim, MD- USA
12. Vikas Khetan, MBBS, MS - India
13. Suganeswari Ganesan, MS - India
14. Andrey Yarovoy, MD - Russia
15. Vera Yarovaya, MD - Russia
16. Elena Kotova, MD - Russia
17. Yacoub A. Yousef, MD - Jordan
18. Kalle Nummi, MD - Finland
19. Tatiana L Ushakova , MD - Russia
20. Olga V Yugay, MD - Russia
21. Vladimir G Polyakov, MD - Russia
22. Marco A Ramirez-Ortiz, MD, MPH - Mexico
23. Elizabeth Esparza-Aguiar, MD - Mexico
24. Guillermo Chantada, MD - Argentina
25. Paula Schaiquevich, MD - Argentina
26. Adriana Fandino, MD - Argentina
27. Jason C. Yam, MD - Hong Kong
28. Winnie W. Lau, MD - Hong Kong
29. Carol P. Lam, MD - Hong Kong
30. Phillipa Sharwood, FRANZCO - Australia
31. Sonia Moorthy, MD - Singapore
32. Quah Boon Long, MD - Singapore
33. Vera Adobea Essuman, MD - Ghana
34. Lorna A. Renner, MD - Ghana
35. Ekaterina Semenova, MD - USA
36. Jaume Català, MD - Spain
37. Genoveva Correa-Llano, MD – Spain
38. Elisa Carreras-Bertran, MD – Spain

Purpose of this Study

- To evaluate the ability of the 8th edition of the American Joint Committee on Cancer(AJCC) Cancer Staging System[1] to estimate retinoblastoma (RB) metastasis-related mortality and globe salvage.
- Comparison with existing classification systems (CHLA[2] and WEH[3]).

1. AJCC = Mallipatna A, Gallie BL, Chévez-Barrios P, et al. Retinoblastoma. In: Amin MB, Edge SB, Greene FL, eds. AJCC Cancer Staging Manual. 8th ed. New York, NY: Springer; 2017:819–831.
2. CHLA = Linn Murphree A. Intraocular retinoblastoma: the case for a new group classification. Ophthalmol Clin N Am. 2005
3. WEH = Shields CL, Mashayekhi A, Au AK, et al. The International Classification of Retinoblastoma predicts chemoreduction success. Ophthalmology. 2006;113(12):2276-2280.

Why AJCC?

1. Multiple RB classification systems predict local treatment outcomes after chemotherapy and not life prognosis.
2. Lack published multi-center validation.
3. Not periodically updated.
4. Different systems used by different centers complicate clinical/research/ literature outcomes.
5. Limited cross-specialty penetration.

1. AJCC: Uses standard TNM (tumor, node, metastasis framework
2. Union for International Cancer Control (UICC) world-wide accepted method of multispecialty cancer staging
3. Standardized data reporting and case-to-case prognostication enabled
4. “First” heritable trait (H) biomarker
5. Approved by the AJCC Ophthalmic Oncology Task Force.

Methods – AJCC-OOTF is “World-Wide”

Internet-based, Retrospective Registry

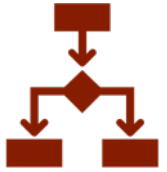
Institutional Review Board and Ethics Approvals were obtained

Study adhered to the Declaration of Helsinki and HIPAA

Methods

Center-specific diagnostic and treatment protocols

Clinical details at presentation



All Classified by AJCC, WEH and CHLA

Treatment details noted

Local treatment failure: need for enucleation or EBRT

Survival outcome: Metastasis and death

Method – Statistical Analysis

- Patient survival and globe salvage data was estimated with the Kaplan-Meier method.

- Cox proportional hazards regression models: associations between treatment outcomes and tumor category.

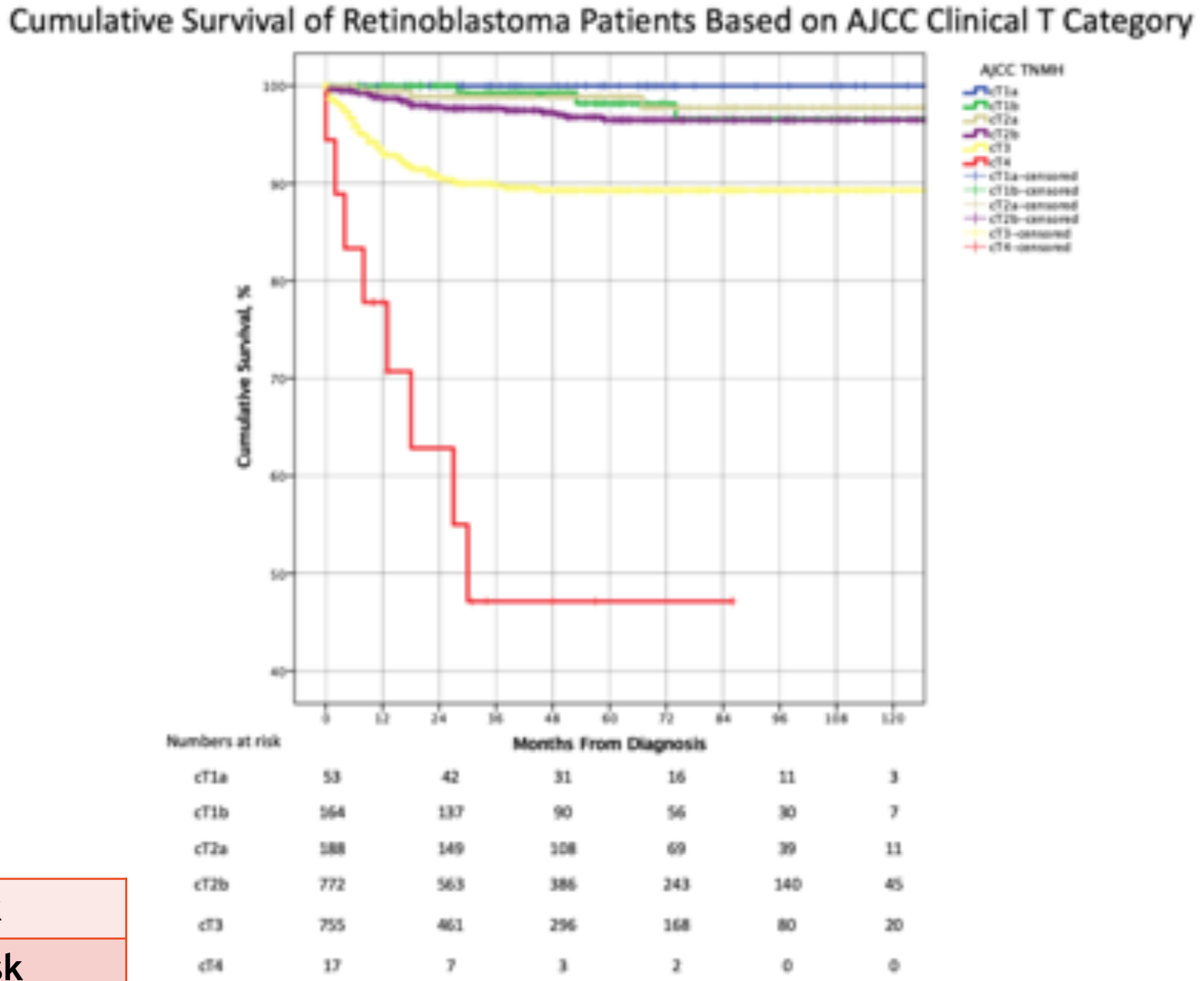
Results

Registry	Eighteen eye cancer specialty centers from 13 countries in over 6 continents
	2190 patients were enrolled between January 2001 and December 2013
	105 patients excluded from analysis due to incomplete data

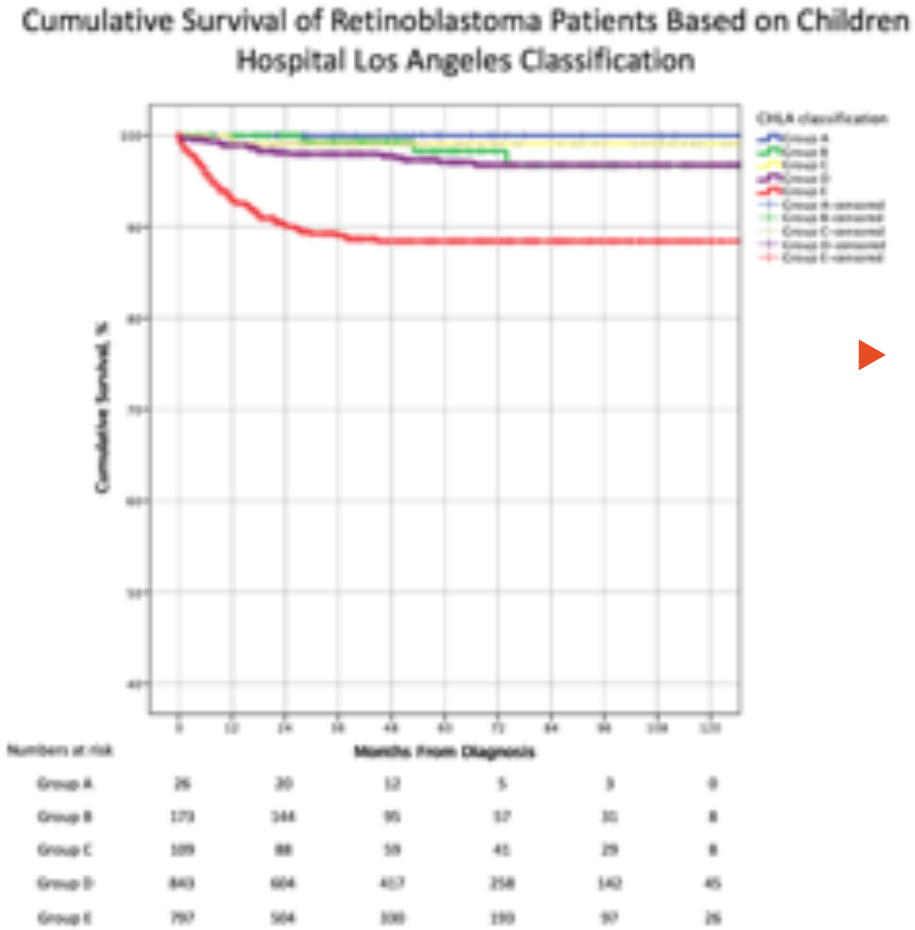
Life Prognosis Analysis

- Median follow-up: 48.0 months
- 109 (5.2%) children developed metastatic disease over a median time- 9.50 months from presentation.
- Cumulative Survival Proportion with respect to tumor categories showed a steep decline from cT1a (100%) to cT4 (45%) at 5-year follow-up

cT3	**8.09-fold risk**
cT4	**48.55-fold risk**



Life Prognosis Analysis

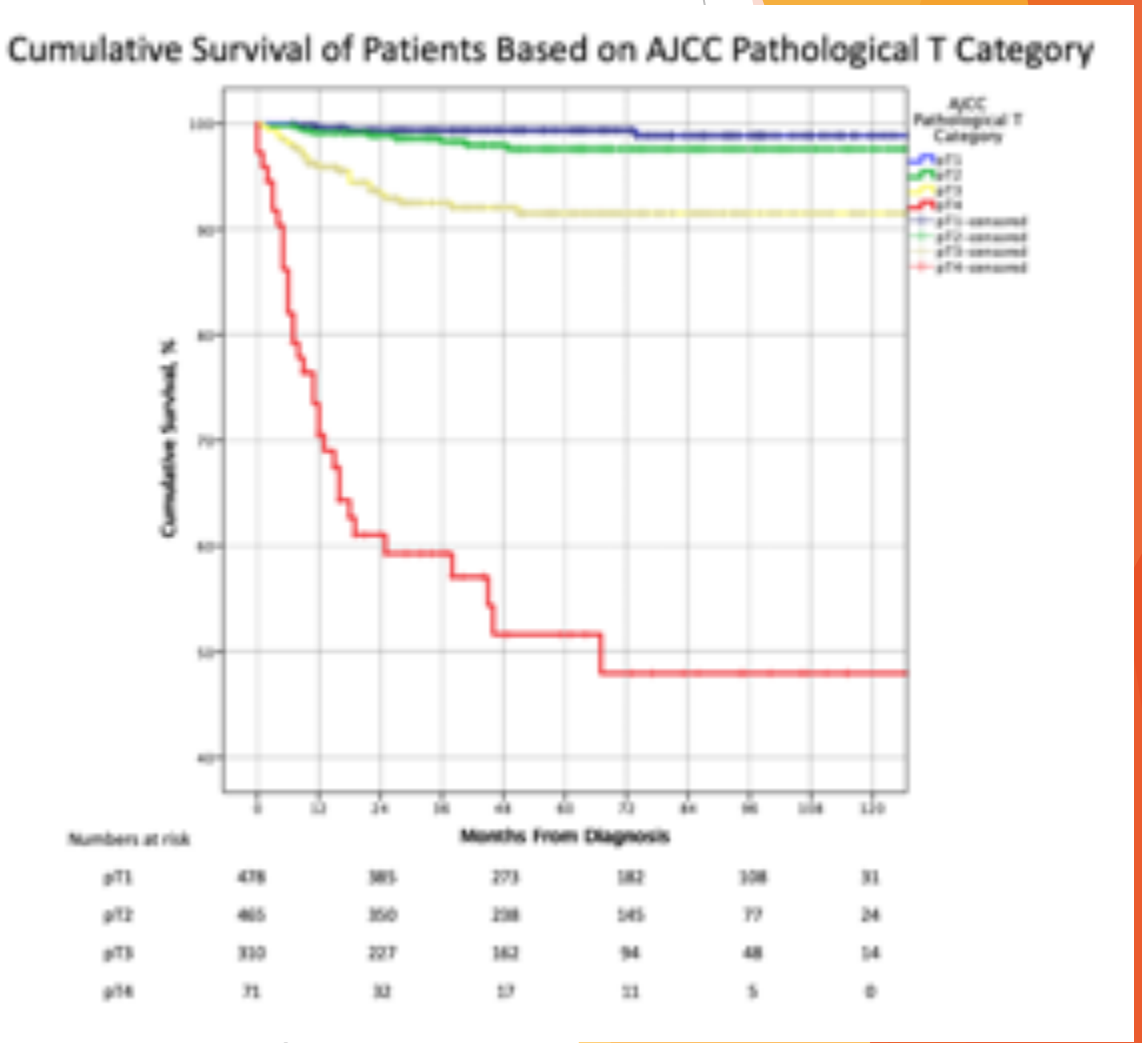


- When compared with CHLA and WEH, AJCC TNMH classification shows a better tumor stratification in terms of risk for metastasis-related mortality.

Life Prognosis by Pathological TNM category in Enucleated Eyes

- Cumulative Survival Proportion with respect to tumor categories showed a steep decline from pT1 (99%) to pT4 (48%) at the 5-year follow-up

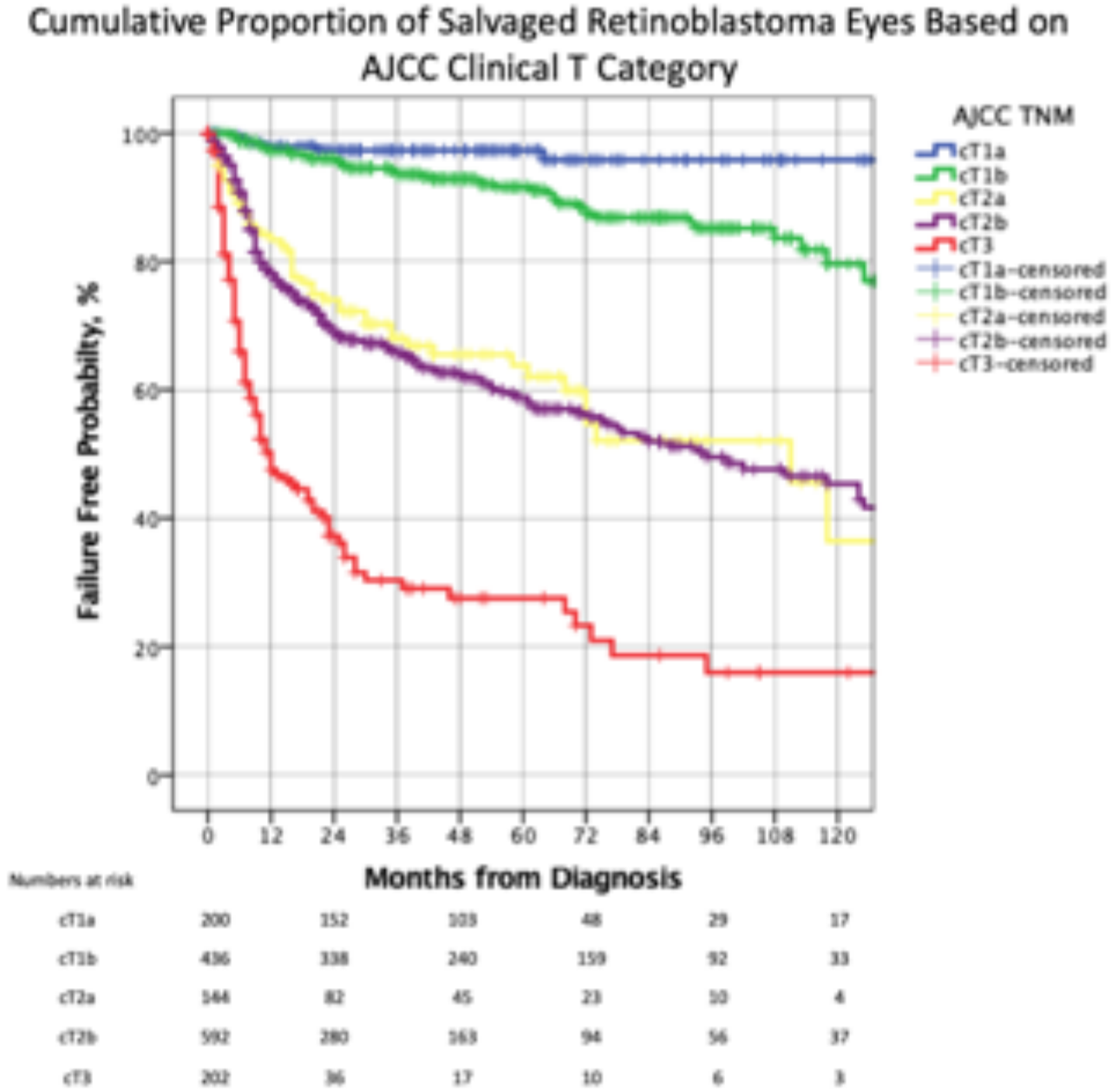
pT3	**9.76-fold risk**
pT4	**77.26-fold risk**



Local Treatment Failure

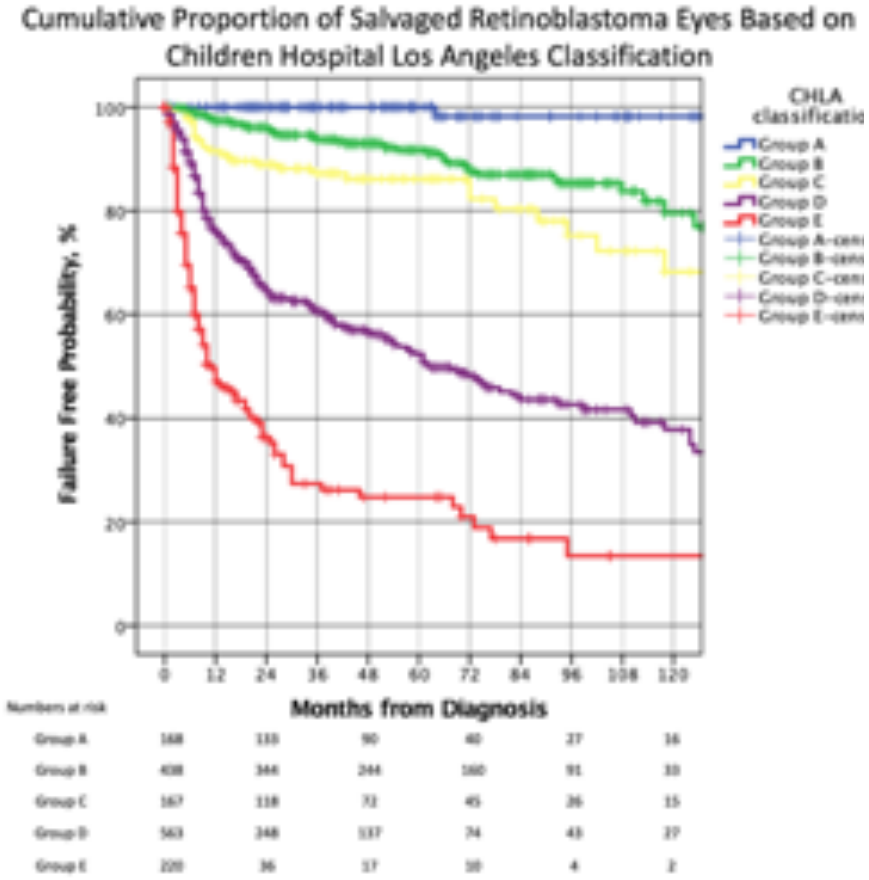
- Of the 2854 eyes, 1574 had an attempt at globe salvage.
- 434 eyes needed enucleation or EBRT.
- As the cT-categories increased from cT1a to cT3, the hazard of treatment failure increased

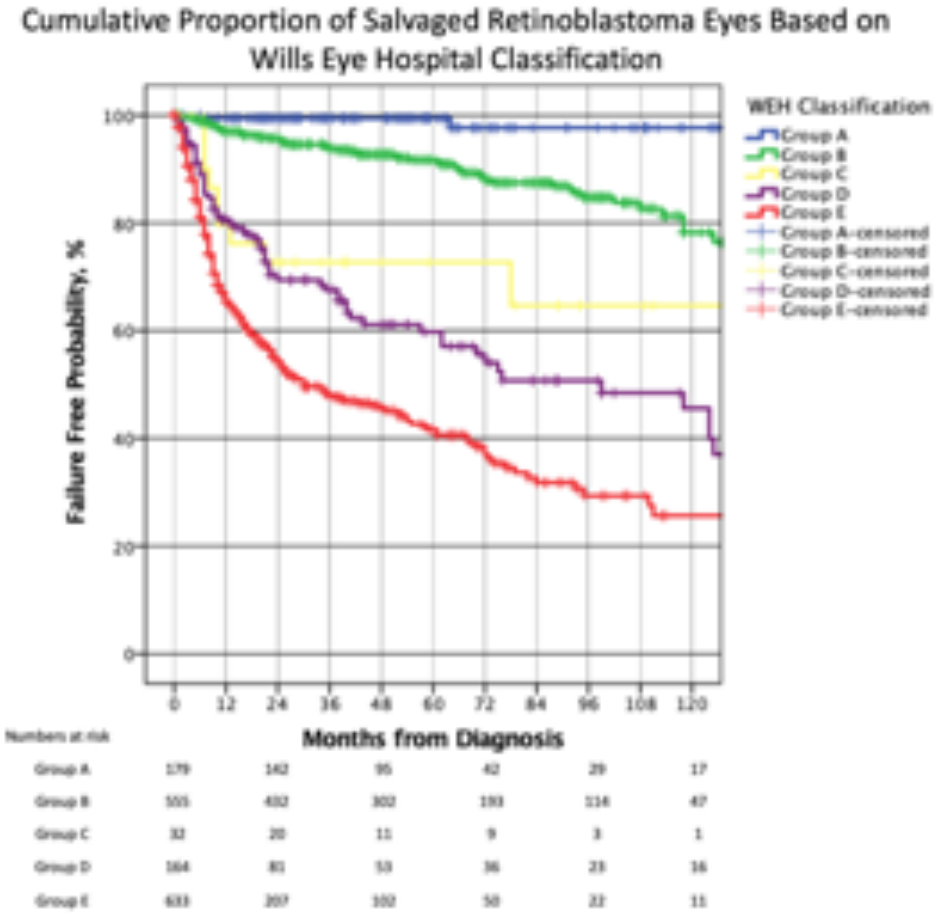
cT1b	**3.5-fold risk**
cT2a	**15.1-fold risk**
cT2b	**16.4-fold risk**
cT3	**45.0-fold risk**



Local Treatment Failure

- Difference in local treatment failure rates was significant in less advanced tumors (cT1a and cT1b) compared to cT3. These results were comparable in CHLA classification.
- But they were in variance with group E in WEH classification.





Discussion

- Multicenter, International, Registry-based studies of rare cancers can be performed using internet-based data sharing. This is the first such study to assess treatment outcome measures in large, heterogenous, real-world retinoblastoma patient population

- AJCC-RB staging predicted metastasis related mortality.

AND

- AJCC-RB staging predicted globe salvage.

AND

- AJCC-UICC staging is the world's multi-specialty cancer language

Summary

- AJCC RB staging:
  - is the only comprehensive classification that predicts metastasis and globe salvage.
  - accounts for both intraocular and extraocular retinoblastoma extent.
  - has been periodically updated with the latest significant medical evidence.
  - holistically includes tumor, nodes, metastasis, and heritable trait.
  - has been adopted by the Union for International Cancer Control (UICC) making it the most common world RB cancer terminology.

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Thanks You.