

RESULTS OF A PROSPECTIVE STUDY FOR THE TREATMENT OF UNILATERAL RETINOBLASTOMA

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Results of a Prospective Study for the Treatment of Retinoblastoma

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- 169 patients, pEFS=0.91
- Patients with **intraocular disease** don't need chemotherapy
- A **shorter regimen** with carboplatin-VP16 alternating with vincristine, CPM, and idarubicin was as effective and less toxic
- No intrathecal is needed
- **Metastatic patients** were not curable

However...

- Intermediate risk: PLONI, microscopical scleral invasion did not so well
- Treatment: Adjuvant carboplatin 500 mg/m² and VP16 100 mg/m² (days 1 and 2) alternating with CPM 40 mg/kg and vincristine 1.5 mg/m²
- 4/13 had an **extraocular relapse** and died
- Metastatic patients died

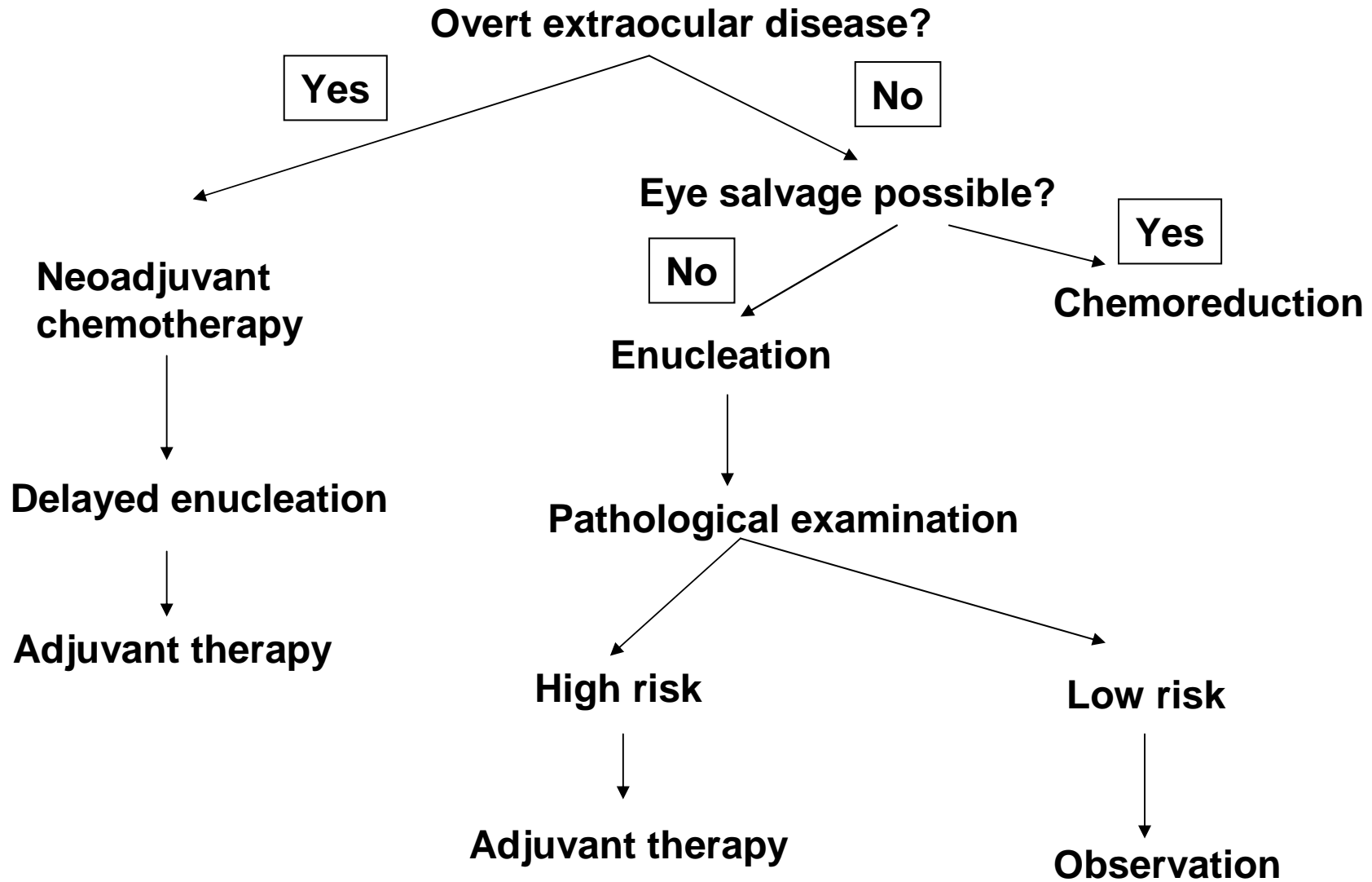
Objectives for this study

- Continue avoiding therapy for **intraocular disease**
- To intensify therapy for **intermediate risk patients**
- To introduce high dose chemotherapy and stem cell rescue for **metastatic patients** (outside the CNS)
- To **reduce toxicity** by using a lower dose of carboplatin

Patients and methods

- Only unilateral patients evaluated
- Prospective study January 2002-December 2007
- Meticulous staging for extraocular disease
- Systematic late sequelae evaluation

Treatment outline



Risk assignment

Lower risk

Intraretinal
Prelaminar
Choroidal
Anterior segment
PLONI and no RF

Higher risk

PLONI and RF
Scleral
Resection margin

Chemotherapy protocol

- Regimen 1

- Vincristine 1.5 mg/m²
- Idarubicin 10 mg/m²
- Cyclophosphamide 65 mg/kg

- Regimen 2

- Carboplatin 500 mg/m² days 1-2
- Etoposide 100 mg/m² days 1-3

Patients with tumor at the resection margin of the optic nerve received orbital radiation 45 Gy

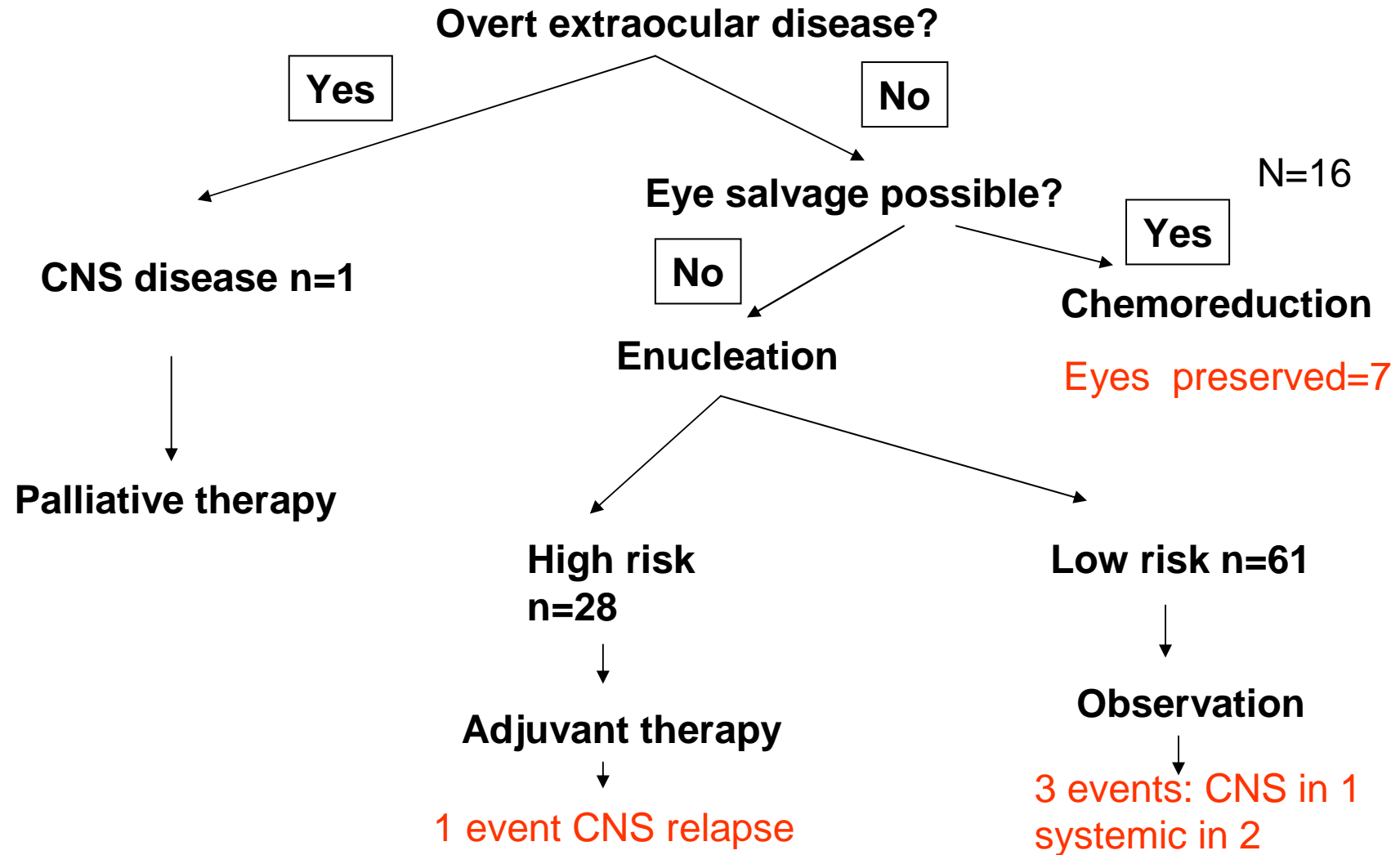
No intrathecal chemotherapy

Total 8 cycles

Results

- 106 evaluable patients
- Median follow up: 31 months
- Median age: 29 months

Results



Outcome after relapse

- Progressive disease after 2nd line therapy=1
- High dose chemotherapy with ASCR in 2nd remission=3 (alive 1)

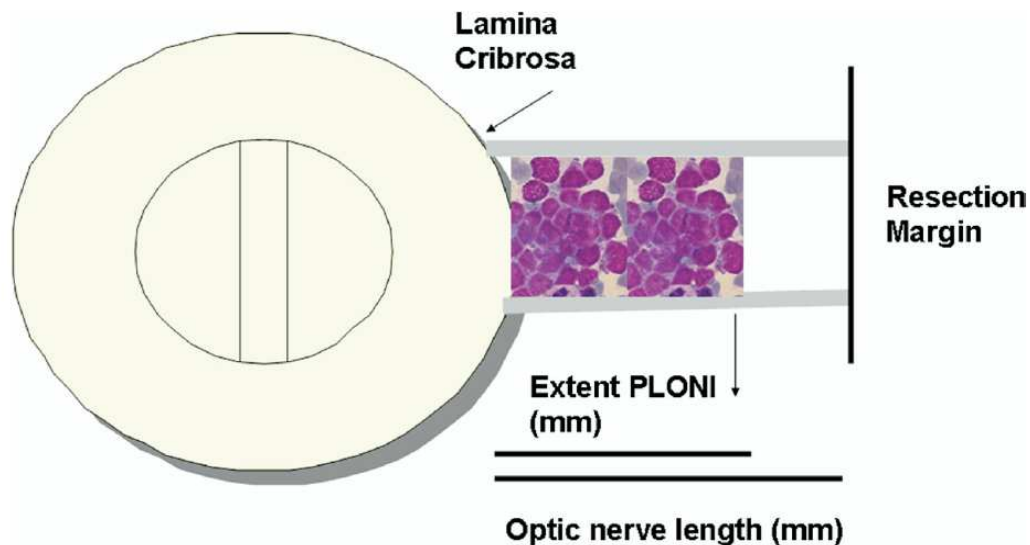
Low risk patients

- 3-year pEFS=0.94
- Intraretinal n=8
- Prelaminar optic nerve n=5
- Isolated choroidal n=37 (full 10)
- PLONI and no other risk factors n=11
- 3 events: 1 isolated choroidal invasion (partial), 2 PLONI

Further refinement of PLONI

Outcome of Patients with Retinoblastoma and Postlaminar Optic Nerve Invasion

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Greater than 20% of overall invasion
More than 1 mm invasion

High risk patients

- 3 year pEFS=0.96
- PLONI and risk factors n=21
- Invasion to resection margin n=5
- Microscopical scleral n=2 (+1 patient with scleral invasion after secondary enucleation)
- Events n=1 (in a patient with invasion to resection margin) CNS relapse and died

Toxicity

- No toxic deaths
- Episodes of fever and neutropenia (median=2)
- Documented infections = 7
- Dose reduction in 1 case
- Transfusions in all but 2 patients
- No other III-IV toxicity
- Late sequelae only in irradiated patients (endocrinopathies n=2)

Conclusions

- pEFS improved
- Our high risk regimen was highly efficacious
- Over 60% of the patients could avoid chemotherapy
- Manageable toxicity

Future steps

- Evaluation of minimally disseminated disease by real time PCR to assign risk for extraocular relapse
- Metastatic patients enrolled on an international study (COG) with ASCR