Age-dependency of the prognostic impact of tumor genomics in localized resectable *MYCN* non-amplified neuroblastomas

Report from the SIOPEN Biology Group on the LNESG Trials

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BACKGROUND

Biology based treatment reduction, i.e. surgery alone also in case of not totally resected tumors, was advised in neuroblastoma patients with localized resectable disease without *MYCN* amplification. However, whether the genomic background of these tumors may influence outcome was unknown and therefore scrutinized in a meta-analysis comprising two prospective therapy studies and a 'validation' cohort.

PATIENTS AND METHODS

Diagnostic samples were derived from 406 INSS stages 1/2A/2B tumors from three cohorts: LNESGI/II and COG. Genomic data were analyzed in two age groups (cut-off: 18 months) and quality controlled by the SIOPEN Biology Group.

RESULTS

In both patient age groups stage 2 tumors led to similarly reduced event-free survival (5y-EFS: 83±3% versus 80±4%), but overall survival was only decreased in patients ≥18m (5y-OS: 97±1% versus 87±4%; p=0.001). In the latter age subgroup, only tumors with SCA led to relapses, with 11q loss as the strongest marker (5y-EFS: 40±15% versus 89±5%; p<0,001). Below 18m, EFS but not OS was decreased only in case of 1p loss (5y-EFS: 62±13% versus 85±3%; p=0,041). SCAs were associated with worse OS only in patients ≥18m but not <18m.

CONCLUSION

The tumor genomic make-up of resectable non-*MYCN* amplified stage 2 neuroblastomas has a distinct age-dependent prognostic impact in neuroblastoma patients. While in the younger age group tumors with unfavourable (SCA) and favorable genetics showed relapses, both without worsening OS, in the older age group only tumors with unfavorable genetics led to relapses and decreased OS.