Predicting outcomes with circulating adrenergic neuroblastoma mRNAs in children with relapsed and refractory neuroblastoma: A BEACON-Neuroblastoma biomarker study.

Abstract

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Abstract Disclosures
**Background:**
Children with relapsed and refractory neuroblastoma (RR-NBL) have poor outcomes. Early identification of children at greatest risk of relapse could mean timelier modifications of treatment to improve outcomes. High levels of adrenergic neuroblastoma mRNAs in blood of children with stage M neuroblastoma receiving frontline treatment predict poor outcome (Viprey PMID: 24590653). Since these markers have not been thoroughly studied in the RR-NBL population, we have prospectively evaluated the prognostic potential of the adrenergic neuroblastoma mRNAs paired-like homeobox 2B (PHOX2B) and tyrosine hydroxylase (TH) in blood from children with RR-NBL treated in the BEACON-Neuroblastoma trial (NCT02308527).

**Methods:**
Blood samples collected at baseline from 88 children were analysed by reverse transcriptase polymerase chain reaction (RTqPCR) for PHOX2B and TH mRNAs. The prognostic power of these mRNAs was evaluated using Kaplan-Meier survival curves and Cox proportional hazards regression. Progression-free (PFS) and overall survival (OS) were calculated from the date that the blood sample was taken at screening to the date of an event; progression, disease recurrence, death or censored alive at the last clinical evaluation.

**Results:**
Of the children in this cohort, 58 (66%) had relapsed and 30 (34%) had refractory disease. Twenty-three (26%) had MYC-N amplified tumours. TH and PHOX2B mRNAs were detected in 55% and 60% of blood samples respectively; the correlation coefficient between TH and PHOX2B was 0.75. Higher levels of TH, PHOX2B mRNAs or both combined were associated with reduced PFS and OS (Table). For TH, median PFS for children with TH levels below the median was 12 months (95%CI, 4.6–13 months) versus 5.5 months (95%CI, 1.8–9.4 months) for those children with TH levels above the median. For PHOX2B, median PFS for children with PHOX2B levels below the median was 11.5 months (95%CI, 7.6–34 months), compared to 5.7 months (95%CI, 1.8–10.5 months) where levels were above the median.

**Conclusions:**
TH and PHOX2B mRNAs in blood collected at baseline identify children with refractory or relapsed neuroblastoma at greatest risk of progression or death. In the RR-NBL
Summary of RTqPCR data for TH and PHOX2B mRNAs in blood (n=87) taken at baseline from children treated in BEACON-Neuroblastoma.

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<th>PFS</th>
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<td></td>
<td>TH</td>
<td>TH and</td>
</tr>
<tr>
<td>Number PCR</td>
<td>TH</td>
<td>PHOX2B</td>
</tr>
<tr>
<td>positive/Total</td>
<td>48/88</td>
<td>52/88</td>
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<td>(% positive)</td>
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