Maintenance Chemotherapy Extends Life for Children With a Rare Cancer – First Treatment Advance for This Cancer in 30 Years

Summary includes data not in the abstract

ASCO Perspective

“By keeping the pressure on this cancer longer with maintenance therapy, we are giving patients two wins – we are boosting cure rates by preventing relapses and doing so with few serious side effects. After three decades of research, this finding goes to show that we will continue innovating treatment, no matter how long it takes,” said ASCO Expert Warren Chow, MD.

CHICAGO – A new chemotherapy strategy improves cure rates for children with rhabdomyosarcoma (a rare cancer of the muscle tissue) who are at high risk for cancer recurrence. In a randomized phase III clinical trial, adding six months of low-dose maintenance chemotherapy after initial treatment increased the 5-year overall survival rate from 73.7% to 86.5%. Children with rhabdomyosarcoma who are alive at five years are considered cured, as tumor recurrence is very rare.

These findings will be presented in ASCO’s Plenary Session, which features four studies deemed to have the greatest potential to impact patient care, out of the more than 5,800 abstracts featured as part of the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting.

“We have been treating rhabdomyosarcoma the same way for more than 30 years, and although different approaches have been tried, this is the first randomized trial in rhabdomyosarcoma to show improved outcomes. By using existing medicines in new ways, we are establishing a new standard of care and, most importantly, we’re helping children and young adults with this rare cancer live longer, with less risk of their cancer returning,” said lead study author Gianni Bisogno, MD, PhD, a professor at the University Hospital of Padova in Italy and Chair of the European Paediatric Soft tissue Sarcoma Study Group.

Related Information
- Read the full abstract
- Meeting presentation information
- More news from the meeting
- Download high-res photo of the study author (coming soon)
- Request an interview

For Your Readers
- Guide to Rhabdomyosarcoma
- Understanding Chemotherapy (Qué es la quimioterapia)
- Understanding Maintenance Therapy
About Rhabdomyosarcoma
Rhabdomyosarcoma originates in the muscle tissue and can occur in any part of the body, but it is most often found in the head, neck, pelvis, and abdomen. Rhabdomyosarcoma is rare, accounting for 4% of all childhood cancers (about 350 children are diagnosed with this cancer each year in the United States).

The prognosis for rhabdomyosarcoma is generally good – 80% of children can be cured with modern treatment, which includes high-dose chemotherapy, radiation, and surgery. However, among children who have metastasis at diagnosis or a recurrence after initial treatment, only 20-30% can be cured.

About the Study
This trial enrolled patients 6 months to 21 years of age who were considered at high risk for recurrence due to having large tumors located in a part of the body that is difficult to treat (e.g., the head).

After completing the standard initial treatment, 371 patients (79% of whom were 10 years old or younger) were randomly assigned to either stop treatment (the former standard of care) or receive six months of maintenance therapy with low doses of two chemotherapy medicines (intravenous vinorelbine and oral cyclophosphamide).

Key Findings
At five years from diagnosis, the disease-free survival (defined as five years without tumor recurrence or death from any cause) was 68.8% in the standard treatment group vs. 77.6% in the maintenance group, and overall survival rates were 73.7% vs. 86.5%, respectively.

The most common side effect in the maintenance group was low blood cell count, though it was usually mild. Febrile neutropenia (a serious side effect involving fever due to very low levels of white blood cells) occurred in 25% of patients. Infection rates were much lower with maintenance treatment than after initial standard chemotherapy, and neurologic side effects resolved after treatment ended. However, as with most kinds of chemotherapy, long-term side effects are still possible, and patients will continue to be monitored.

Next Steps
The findings of this trial have already changed the standard of care in Europe, where investigators shared the results with soft tissue sarcoma study group institutions in 14 countries. As the standard of care is somewhat different in the United States, there is a need for further study to understand how to integrate maintenance therapy into existing treatment protocols.

This study received funding from Fondazione Città della Speranza, Italy.

Study at a Glance

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pediatric Rhabdomyosarcoma</th>
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<tbody>
<tr>
<td>Trial Phase, Type</td>
<td>Phase III, Randomized</td>
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<tr>
<td>Patients on Trial</td>
<td>371</td>
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<tr>
<td>Intervention Tested</td>
<td>Standard Treatment plus Maintenance Chemotherapy vs. Standard Treatment</td>
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<tr>
<td>Primary Finding</td>
<td>mDFS at 5 years 77.6% vs. 69.8%; mOS at 5 years 86.5% vs. 73.7%</td>
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**2018 ASCO Annual Meeting: Presentation Information**

**Plenary Session Including the Science of Oncology Award and Lecture**

**Sunday, June 3, 2018: 2:15-2:30 p.m. CT**

McCormick Place, Hall B1

Gianni Bisogno, MD
Department of Women and Children Health, University Hospital of Padova
Padova, Italy

About ASCO:
Founded in 1964, the American Society of Clinical Oncology, Inc. (ASCO®) is committed to making a world of difference in cancer care. As the world’s leading organization of its kind, ASCO represents nearly 45,000 oncology professionals who care for people living with cancer. Through research, education, and promotion of the highest-quality patient care, ASCO works to conquer cancer and create a world where cancer is prevented or cured, and every survivor is healthy. ASCO is supported by its affiliate organization, the Conquer Cancer Foundation. Learn more at [www.ASCO.org](http://www.ASCO.org), explore patient education resources at [www.Cancer.Net](http://www.Cancer.Net), and follow us on [Facebook](http://Facebook), [Twitter](http://Twitter), [LinkedIn](http://LinkedIn), and [YouTube](http://YouTube).

**Abstract LBA2:** Maintenance low-dose chemotherapy in patients with high-risk (HR) rhabdomyosarcoma (RMS): A report from the European Paediatric Soft Tissue Sarcoma Study Group (EpSSG).

**Authors:** Gianni Bisogno, Gian Luca De Salvo, Christophe Bergeron, Meriel Jenney, Johannes H.M. Merks, Veronique Minard-Colin, Daniel Orbach, Heidi Glosli, Julia Chisholm, Michela Casanova, Soledad Gallego Melcon, Andrea Ferrari, European Paediatric Soft tissue sarcoma Study Group (EpSSG); Department of Women and Children Health, University Hospital of Padova, Padova, Italy; Clinical Trials and Biostatistics Unit, Veneto Institute of Oncology-IRCCS, Padua, Italy; Institut d'Hematologie et d'Oncologie Pédiatrique, Centre Léon Bérard, Lyon, France; Department of paediatric oncology, Children’s Hospital for Wales, Cardiff, GB; Emma Children’s Hospital-Academic Medical Center (EKP-AMC), Amsterdam, Netherlands; Gustave Roussy, Villejuif, France; Institut Curie, Paris, France; Department of Paediatric and Adolescent Medicine, Oslo University Hospital, Oslo, Norway; Children and Young People’s Unit, The Royal Marsden NHS Foundation Trust, Sutton, United Kingdom; Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; University Hospital Vall d’Hebron, Barcelona, Spain; Istituto Nazionale per lo Studio e la Cura dei Tumori - IRCCS, Milan, Italy

**Background:** Most patients with localized RMS achieve complete remission during standard (std) treatment but approximately 20-30% of them relapse and chance of salvage is poor. We tested whether adding maintenance metronomic chemotherapy after std chemotherapy would improve survival for patients with non metastatic RMS defined as HR according to EpSSG stratification.

**Methods:** Patients (pts) age >6 months <21 years, with N0 alveolar (A)RMS or incompletely resected (Group II or III) embryonal (E)RMS arising in an unfavorable primary site and/or N1 in complete remission after std treatment including 9 cycles of ifosfamide, vincristine and actinomycin D +/- doxorubicin, surgery and/or radiotherapy were eligible for randomization to stop treatment (Std-arm) or receive maintenance chemotherapy (M-arm) with 6 28-day cycles of iv vinorelbine 25 mg/m² on day 1,8,15 of each cycle and continuous daily oral cyclophosphamide 25 mg/m² . The study was initially designed with 80% power (5% 2-sided alpha level) to detect an increase in 3 yr Event Free Survival (EFS) from 55% to 67%, a Hazard Ratio of 0.67, but was successively amended to allow a detection of a relative reduction in the relapse rate of 50% in the M-arm, with 80% power, testing at the 5% significance level (2-sided).

**Results:** 670 pts were entered between 4/2006-12/2016, with 371 confirmed eligible and 186 assigned to the std-arm and 185 to M-arm. Clinical features were well balanced in the two arms and included ERMS 67%, ARMS 33%, age 10+
years 21%; IRS Group III 86%; N1 16%. Most common primary tumor sites were parameningeal (32%) and “other” sites (23%). With median follow up of 5 years in surviving pts, 3 yr EFS and overall survival (OS) in M-arm vs Std-arm were respectively: EFS 78.4% (95% IC 71.5-83.8) vs 72.3% (95% IC 65.0-78.3) (p = 0.061) and OS 87.3% (95% IC 81.2-91.6) vs 77.4 (95% IC 70.1-83.1) (p = 0.011). Toxicity in the M-arm was manageable: grade 3/4 febrile neutropenia in 25% of pts, grade 4 neurotoxicity in 1.1%. **Conclusions:** The addition of maintenance after std treatment significantly improves OS in HR RMS patients and support its inclusion in future EpSSG trials.

**Disclosures:** Gianni Bisogno, MD, Consulting or Advisory Role with Clinigen Group, Travel, Accommodations, Expenses from Jazz Pharmaceuticals; Gian Luca De Salvo, MD, Travel, Accommodations, Expenses from Bayer; Soledad Gallego Melcon, MD, Consulting or Advisory Role with Clinigen Group