Seźary Syndrome: Clinicopathological and Immunophenotypical Characteristics and Outcomes

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Disclosure

• Alexion: Speakers Bureau
• Celgene: Speakers Bureau
• Seattle Genetics: Speakers Bureau
Mycosis fungoides (MF) /Sézary syndrome (SS) are rare malignant T-cell lymphoproliferative disorders derived from mature CD4+ T-helper/inducer cells.

SS is distinguished differently from MF by the presence of 1000 or more abnormal cerebriform lymphocytes in the peripheral blood.
SEZARY CELL

- Scant light blue cytoplasm
- Nucleoli usually absent
- Irregular nuclear membrane (cerebriform nucleus: looks like "brain")
Clinical Manifestations

• Generalized erythroderma covering 80% of the body
  • Patches
  • Plaques
  • Tumors
• Severe pruritus/ Frequent Staph. Aureus infections
  • Generalized lymphadenopathy
  • Alopecia
  • Palmoplantar hyperkeratosis
  • Onychodystrophy
  • Ectropion
Multimodality therapy

- Extracorporeal photopheresis
- Interferon alpha, alemtuzumab,
- Histone deacetylase (HDAC) inhibitors
- Monochemotherapy
Between 2002 and 2015, 50 Pts with SS were evaluated and treated at Moffitt Cancer Center (MCC).

Patient demographics, disease and treatment characteristics, responses and outcomes were collected from CTCL database.

We characterized pts based on immunophenotype into 4 groups based on aberrant loss of CD26 and CD7 or both.
Response to treatment were assessed using standard criteria: complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD).

Descriptive statistics were used to report baseline characteristics. Chi square and t-test were used for comparison of categorical and continuous variables respectively. Kaplan-Meier estimates of OS.
Results

- We identified 50 patients with SS with median follow-up of 52 months.
- Median age was 70 years.
- Male to female ratio was 1.6:1.
- Most Pts were Caucasians (88%).
- A majority of patients (76%) had advanced stage disease (IVA+IVB).
- Measurable adenopathy was identified in 35 patients (70%).
- Median number of Seźary cell count in peripheral blood was 1,747/ul.
<table>
<thead>
<tr>
<th>Treatments</th>
<th>Results</th>
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<tbody>
<tr>
<td>Extracorporeal Photopheresis</td>
<td>ORR 24%, CR 86%</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>ORR 8%, CR 6%</td>
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<tr>
<td>MTX</td>
<td>ORR 6%, CR 2%</td>
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<tr>
<td>Bexarotene</td>
<td>ORR 10%, CR 2%</td>
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<tr>
<td>Romidepsin</td>
<td>ORR 6%, all PR</td>
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<td>Vorinostat</td>
<td>ORR 4%, CR 2%</td>
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<tr>
<td>Interferon</td>
<td>ORR 6%, CR 2%</td>
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Figure 1 KM estimates for OS: median OS was 96 mo (95%CI 52-139)
Kaplan Meier Estimate based on Immunophenotype

Figure 2  KM estimates for OS based on immunophenotype pattern

Pts were categorized as:
CD4+CD26- 13 (26%),
CD4 + CD 7- in 6 (12%),
CD4+CD26-CD7- in 17 (34%),
and CD4+CD26+CD7+ in 12 (24%).

The median OS for CD26 – CD 7 – was 84 mo compared to other groups.
This was significant comparing to CD7 – (p =0.05), and CD 26 + CD 7 + (p 0.02)
but only a trend compared to CD26 – (p 0.3).
Figure 3 KM estimates for OS based on Sezary cell count:
The median OS was 86 month if absolute Sezary cell count was $\geq$ 1700 compared to 96 mo if < 1700 , p=0.4.
• Patients with SS showed improved survival compared to historical studies. Advent of ECP, novel targeted molecules such HDAC inhibitors and alemtuzumab, earlier diagnosis and better supportive care most probably contributed to this phenomenon.
• Except ECP, CR are very rare.

• A majority of patients requires multimodality induction therapy followed by maintenance therapy.

• Pts with Seźary cell population characterized by aberrant loss of both CD26 and CD7 had worse outcomes.

• There was also a tendency for worse OS with higher circulating absolute SS count.
“Sí, se puede.”

“This history of the United States and Cuba encompass revolution and conflict; struggle and sacrifice; retribution and now, reconciliation. It is time now, for us to leave the past behind. It is time for us to look forward to the future together.”

-President Obama