LUNG CANCER UPDATES
IASLC HIGHLIGHTS
7-10 DE SEPTIEMBRE 2019
BARCELONA
Cáncer de pulmón no microcítico localizado y localmente avanzado

Dra. Anna Estival González
Early and Locally advanced NSCLC

- Phase II, prospective single-arm study of adjuvant pembrolizumab in N2 positive non-small cell lung cancer treated with neoadjuvant concurrent chemoradiotherapy followed by curative resection: Preliminary results.
- Adjuvant Chemotherapy +/- Bevacizumab for early stage NSCLC: Updated chemotherapy subset analysis
- Durvalumab impact in the treatment strategy of stage III Non-Small Cell Lung Cancer (NSCLC): an EORTC Young Investigators Lung Cancer Group survey
Phase II, prospective single-arm study of adjuvant pembrolizumab in N2 positive non-small cell lung cancer treated with neoadjuvant concurrent chemoradiotherapy followed by curative resection: Preliminary results.

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Phase II, prospective single-arm study of adjuvant pembrolizumab in N2 positive non-small cell lung cancer treated with neoadjuvant concurrent chemoradiotherapy followed by curative resection: Preliminary results.

**Study design**

- **Neoadjuvant CCRT with Weekly paclitaxel/cisplatin**
- **Surgery**
- **Adjuvant treatment**

- Locally advanced NSCLC clinical stage IIIA-N2
- Cisplatin 25mg/m2 once weekly
- Paclitaxel 50mg/m2 once weekly
- Radiotherapy 44Gy/22Fx for 5 weeks

- Pembrolizumab 200mg IV q 3weeks for 24months

**Study endpoints**

- 1’ Endpoint: Disease free survival (DFS)
- 2’ Endpoints: OS, adverse events (AEs), the correlation between PD-L1 expression and the efficacy (DFS, OS)

**Key inclusion criterias**

- Be within 6 weeks after complete resection after neo-adjuvant CCRT
- Have performance status of 0 or 1 on the ECOG PS
- Patients who complete neoadjuvant CCRT regimen
- Be willing to provide tissue from a obtained before neoadjuvant CCRT and surgical specimen
- Patients with adequate organ function

**Key exclusion criterias**

- Every 12 weeks for the 1st year, every 16 weeks for the 2nd year, every 6 months for the 3rd year, every year thereafter

Total number of trial subjects: **37 patients**
Estimated enrollment period: **15 months**
The estimated average length of treatment per patient: **24 months**
The expected study periods: **51 months**
The final analyses: **When 22 patients experience event (progression or death)**
Phase II, prospective single-arm study of adjuvant pembrolizumab in N2 positive non-small cell lung cancer treated with neoadjuvant concurrent chemoradiotherapy followed by curative resection: Preliminary results.

RESULTS

Current status and survival analyses of study population (n=37)

- Median duration of f/u (range): 11.7 months (2.9 – 16.8), 12 months DFS rate was 66.1%
- 54.1% of patients are still on treatment.
- Median disease-free survival: Not reached
- 11 cases of PD event (EGFR mutation [n=3], pN2 [n=9], pN0 [n=2], adenocarcinoma [n=8])
- Sites of PD: lung (n=2), brain (n=7), lymph node (n=2), liver (n=2), bone (n=1).

Expression profile of PD-L1 (22C3) immunohistochemistry (IHC)

<table>
<thead>
<tr>
<th></th>
<th>Pre-C CRT sample (n=21)</th>
<th>Surgical sample (n=27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-L1 ≥ 50%</td>
<td>1 (4.8%)</td>
<td>5 (18.5%)</td>
</tr>
<tr>
<td>50 %&gt; PD-L1 ≥ 1%</td>
<td>5 (23.8%)</td>
<td>9 (33.3%)</td>
</tr>
<tr>
<td>1% &gt; PD-L1</td>
<td>15 (71.4%)</td>
<td>13 (48.2%)</td>
</tr>
<tr>
<td>Samples with paired result</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased after CCRT</td>
<td>N=14</td>
<td></td>
</tr>
<tr>
<td>Decreased after CCRT</td>
<td>7 (50.0%)</td>
<td>2 (14.3%)</td>
</tr>
<tr>
<td>No change after CCRT</td>
<td>5 (35.7%)</td>
<td></td>
</tr>
</tbody>
</table>
Adjuvant Chemotherapy +/- Bevacizumab for early stage NSCLC: Updated chemotherapy subset analysis

Heather A. Wakelee on behalf of ECOG-ACRIN


1Stanford University, Stanford, CA/USA, 3Dana Farber Cancer Institute, Boston/USA, 4Albert Einstein College of Medicine, Bronx, NY/USA, 5Thomas Jefferson University, Philadelphia/USA, 6Rutgers Cancer Institute of New Jersey, Newark/USA, 7University of Pittsburgh, Pittsburgh/USA, 8University of Chicago, Chicago, IL/USA 9MN Oncology, Maplewood/USA 10Ireland Cooperative Oncology Research Group, Dublin/Ireland, 11Heartland Cancer Research, Saint Louis/USA 12Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY/USA, 13Southeast Clinical Oncology Research Consortium, Winston-Salem/USA, 14University of Wisconsin Carbone Cancer Center, Madison, WI/USA 15University of Pennsylvania, Philadelphia/USA, 16Vanderbilt-Ingram Cancer Center, Nashville, TN/USA 17State University of New York Upstate Medical University, Syracuse/USA 18UC Davis Comprehensive Cancer Center, Sacramento, CA/USA 19Mayo Clinic, Rochester, MN/USA, 20University of Alberta, Edmonton/Canada, 21Princess Margaret Cancer Centre, Toronto/Canada, 22Emory University School of Medicine, Atlanta, GA/USA 23University of Virginia Health System, Charlottesville, VA USA
Adjuvant Chemotherapy +/- Bevacizumab for early stage NSCLC: Updated chemotherapy subset analysis

Schema - phase III

ELIGIBLE:
- Resected
- Stage IB (≥ 4 cm)-IIIA

STRATIFIED:
- Cisplatin Doublet*
- Stage
- Histology
- Sex

Randomize 1:1

Arm A:
Chemotherapy
X 4 cycles*

Arm B:
Chemotherapy
x 4 cycles*
+ Bevacizumab
x 1 year

*Investigator Choice of 4 chemotherapy regimens:
1501 enrolled 7/07-9/13
21 day cycles all with Cisplatin given at 75 mg/m² on day 1

Cisplatin/Vinorelbine: 30 mg/m² d 1, 8 (25.0%); 83.5 mo f/up
Cisplatin/Docetaxel: 75 mg/m² d 1 (22.9%); 89.9 mo f/up
Cisplatin/Gemcitabine: 1200 mg/m² d1,8 (18.9%); 87.8 mo f/up
Cisplatin/Pemetrexed: 500 mg/m² d 1 (33.2%); 71.9 mo f/up

Bevacizumab 15 mg/kg IV q 3 weeks for up to 1 year

Followed for:
- Survival/Recurrence
- CXR/exam q 3 months x 2y, q 6 m through year 5, then annually through year 10
Adjuvant Chemotherapy +/- Bevacizumab for early stage NSCLC: Updated chemotherapy subset analysis

DFS and OS by chemotherapy by histology (Pooled regardless of Bev arm)

OS by Chemo type, **Non-Squamous** Patients
(Pooled across arm A+ B (regardless of Bev))

<table>
<thead>
<tr>
<th>Chemo type</th>
<th>N</th>
<th>Median (mos)</th>
<th>0.95 lower CI</th>
<th>0.95 upper CI</th>
<th>Log-rank P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cis/Doce</td>
<td>202</td>
<td>80</td>
<td>66.9</td>
<td>108</td>
<td>0.346</td>
</tr>
<tr>
<td>Cis/Gem</td>
<td>134</td>
<td>97.8</td>
<td>62.6</td>
<td>NA</td>
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<tr>
<td>Cis/Pem</td>
<td>494</td>
<td>98.8</td>
<td>89</td>
<td>NA</td>
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<tr>
<td>Cis/Vin</td>
<td>248</td>
<td>92.4</td>
<td>75</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

OS by Chemo type, **Squamous** Patients Only
(Pooled across arm A+ B (+/- Bev))

<table>
<thead>
<tr>
<th>Chemo type</th>
<th>N</th>
<th>Median (mos)</th>
<th>0.95 lower CI</th>
<th>0.95 upper CI</th>
<th>Log-rank P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cis/Doce</td>
<td>143</td>
<td>109</td>
<td>86.2</td>
<td>NA</td>
<td>0.95</td>
</tr>
<tr>
<td>Cis/Gem</td>
<td>151</td>
<td>98</td>
<td>86.4</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Cis/Vin</td>
<td>128</td>
<td>119</td>
<td>75.4</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>
Adjuvant Chemotherapy +/- Bevacizumab for early stage NSCLC: Updated chemotherapy subset analysis

OS by chemotherapy regimen +/- BEV, by histology

**VIN**
- HR 1.11, p.58

**DOCE**
- HR 1.28, p.217

**VIN**
- HR 1.22, p.493

**DOCE**
- HR 1.19, p.506

**GEM**
- HR 1.43, p.171

**PEM**
- HR 0.65, p.00368

**GEM**
- HR 0.8, p.385

Significant positive improvement in DFS + OS with bev added to pemetrexed

Trends of worse outcomes with bev added to docetaxel or vinorelbine
Durvalumab impact in the treatment strategy of stage III Non-Small Cell Lung Cancer (NSCLC): an EORTC Young Investigators Lung Cancer Group survey


1 CHU Grenoble Alpes, Grenoble, France; 2 EORTC, Bruxelles, Belgium; 3 Institut Jules Bordet, Bruxelles, Belgium; 4 University Hospital of Modena, Modena, Italy; 5 Maastricht University Medical Centre, Maastricht, Netherlands; 6 IRCCS Sacro Cuore Don Calabria Hospital, Verona, Italy; 7 Northern General Hospital, Sheffield, United Kingdom; 8 The Christie-University of Manchester, Manchester, United Kingdom; 9 Institut Curie, Paris, France; 10 Centre Leon Berard, Lyon, France; 11 AP Marseille, Marseille, France; 12 Institut Gustave Roussy, Paris, France; 13 San Luigi Gonzaga Hospital, Turin, Italy; 14 Royal Marsden Hospital, London, United Kingdom; 15 Lungen Clinic, Grosshansdorf, Germany; 16 Instituto Oncologico Veneto, Padova, Italy
Durvalumab impact in the treatment strategy of stage III Non-Small Cell Lung Cancer (NSCLC): an EORTC Young Investigators Lung Cancer Group survey

- 96% of cases consider concurrent CHT-RT the best strategy for stage III unresectable fit patients

Percentage of concomitant treatment for centre

Chemotherapeutic strategy associated with concomitant radiotherapy

Beginning of durva after CHT-RT

PDL1 expression and treatment strategy

Rebiopsy after CHT-RT in case of PD-L1<1%
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