Lung cancer immunotherapy

- Introduction: immunotherapy
- Lung cancer vaccination
- Lung cancer immunomodulation
- Conclusion
Cancer immunotherapy
> a bit of history...

- Exploit capacity of the immune system to recognize and destroy tumours
- 1890s: Coley’s toxins, first cancer treatment vaccine derived from dead bacteria
- Immunotherapies offer the promise of prolonging survival with limited toxicity
  - Limited success of immunotherapies in initial clinical trials in solid tumours
  - Renewed interest with ipilimumab for melanoma and sipuleucel-T for prostate cancer

Dr William Coley: pioneer of cancer immunotherapy


Lung cancer immunotherapy
> what?

Cancer immunotherapy: any interaction with the immune system to treat cancer

Active: priming of the immune system
- Antigen-specific
  - Antigen-specific antibodies & cytotoxic T cells
- Non-antigen-specific
  - Enhancement of immune system: cytokines, checkpoint inhibitors

Passive: delivery of compounds that may use immune system
- Monoclonal antibodies
  - Cetuximab, trastuzumab, ...
- Adoptive cell transfer
  - T cells, CARs, ...

Cancer vaccination therapy
Cancer immunomodulation therapy
Targeted antibodies immunotherapy
Cellular immunotherapy
Lung cancer immunotherapy > for which patients?

- Immunotherapies traditionally considered more appropriate for low burden disease (e.g. early – locally advanced NSCLC)

- Recent positive findings in advanced tumours as well
  - Ipilimumab immunomodulator for advanced melanoma
  - Sipuleucel-T dendritic cell vaccine for metastatic hormone-refr. prostate cancer


Lung cancer immunotherapy

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- Lung cancer immunomodulation
- Conclusion
Lung cancer vaccination > components

**Antigen(s)**
- tumour cells
  - autologous
  - allogeneic
- peptides
- full proteins
- gangliosides
- DNA

**Adjuvants**
- chemical
  - Phospholipids, aluminium, ...
- biological
  - TGF-β blockade, ...
- viral vectors
- dendritic cells
- liposomes

Lung cancer vaccination > NSCLC ongoing ph3 trials

<table>
<thead>
<tr>
<th>Setting</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early stage</td>
<td></td>
</tr>
<tr>
<td>Post surgery</td>
<td></td>
</tr>
<tr>
<td>Loc. adv. stage</td>
<td></td>
</tr>
<tr>
<td>Post chemorad</td>
<td></td>
</tr>
<tr>
<td>Advanced</td>
<td></td>
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<tr>
<td>In combo with chemo</td>
<td></td>
</tr>
<tr>
<td>MAGE-A3 ASCI</td>
<td></td>
</tr>
<tr>
<td>MAGRIT target 2270 recruited</td>
<td></td>
</tr>
<tr>
<td>Tecemotide (L-Blp25)</td>
<td></td>
</tr>
<tr>
<td>START target 1300 reported ASCO 13</td>
<td></td>
</tr>
<tr>
<td>Belagenpumatucel-L</td>
<td></td>
</tr>
<tr>
<td>STOP target 700</td>
<td></td>
</tr>
<tr>
<td>rEGF target 1000</td>
<td></td>
</tr>
<tr>
<td>ongoing</td>
<td></td>
</tr>
<tr>
<td>TG4010</td>
<td></td>
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<tr>
<td>TIME target 1000</td>
<td></td>
</tr>
<tr>
<td>ongoing</td>
<td></td>
</tr>
<tr>
<td>Racotumomab (1E10)</td>
<td></td>
</tr>
<tr>
<td>target 1082</td>
<td></td>
</tr>
<tr>
<td>ongoing</td>
<td></td>
</tr>
</tbody>
</table>

N ~ 8,000
Lung cancer vaccination > NSCLC ongoing ph3 trials

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<td>Tecemotide (L-BLP25) START target 1500 reported ASCO 13</td>
</tr>
<tr>
<td>Loc. adv. stage</td>
<td>Belagenpumatucel-L STOP target 700 reported ESMO 13</td>
</tr>
<tr>
<td>Post chemorad</td>
<td>rEGF target 1000 ongoing</td>
</tr>
<tr>
<td>Advanced</td>
<td>TG4010 TIME target 1000 ongoing</td>
</tr>
<tr>
<td>In combo with chemo</td>
<td>Racotumomab (1E10) target 1082 Ongoing</td>
</tr>
</tbody>
</table>

- compound
- ph2 data
- ph3 development / data
- predictive biomarker?

Lung cancer vaccination > compound: MAGE-A3 ASCI

- Antigen
  - MAGE-A3 protein, not expressed in normal cells, expressed in 35% of early stage NSCLC*

  ![Prot D | MAGE-A3 | His-tail]
  
  - Prot D: 109 aa
  - MAGE-A3: 312 aa
  - His-tail: 7 aa

- Adjuvant
  - GSK proprietary adjuvant system (AS02B)
  - in oil-in water emulsion

- Administration
  - i.m. / q3w x5 -> q3m x8 (27 months in total)

Lung cancer vaccination > ph2: randomised MAGE-A3 trial

Resected NSCLC
- p-stage IB / II
- complete resection
- MAGE-A3 rt PCR +
- PS 0-1

N=122

MAGE-A3 ASCI 300 µg i.m.
q3w x5 -> q3m x8 (27 m total)

N=60

Placebo
same schedule

Primary endpoint: disease-free interval

Vansteenkiste et al., J Clin Oncol 31: 2396-2403, 2013

Lung cancer vaccination > ph2: MAGE-A3 disease-free interval

DFI: Interval from the date of surgical resection to the date recurrence

Median FU 44 mo

HR = 0.75 (95%CI 0.46 – 1.23)
One-sided logrank P = 0.122

MAGE-A3 vaccination > biomarker? experience in melanoma

- Gene profiling as optional exploratory research
- Tumor biopsies taken prior to MAGE-A3 immunization
- Affymetrix platform: HG-U133. Plus 2.0 gene chips

Prediction of clinical benefit?


MAGE-A3 vaccination > biomarker? randomised ph2 NSCLC

HR (GS+) = 0.42 (95%CI 0.17-1.03)
HR (GS-) = 1.17 (95%CI 0.59-2.31)

Disease-free interval

MAGE-A3 vaccination > **biomarker?** randomised ph2 NSCLC

- HR (GS+) = 0.42 (95% CI 0.17-1.03)
- HR (GS-) = 1.17 (95% CI 0.59-2.31)

- Validation across
  - tumour type: melanoma -> lung
  - stage: advanced -> early
- Further validation in ph3

Validation across:
- tumour type: melanoma -> lung
- stage: advanced -> early
- Further validation in ph3

Lung cancer vaccination > **ph3:** MAGE-A3 MAGRIT trial

- MAGE-A3 as Adjuvant Non-Small Cell Lung Cancer Immunotherapy
  - worldwide multicenter, randomized, double-blind, placebo-controlled ph III trial
  - expected N=10,000 screened -> N=2270 patients randomized
  - primary endpoint: disease-free survival

**Resected MAGE-A3 (+) NSCLC**

- Decision for chemo
- No chemo

- Up to 4 cycles of chemo
- Randomisation 2:1
  - MAGE-A3 immunotherapy
  - Placebo

- Randomisation 2:1
  - MAGE-A3 immunotherapy
  - Placebo

Clinicaltrials.gov NCT00480025


Ulloa-Montoya et al., J Clin Oncol 31: 2388-2395, 2013
Lung cancer vaccination > ph3: MAGE-A3 MAGRIT trial

MAGE-A3 as Adjuvant Non-Small Cell Lung Cancer ImmunoTherapy
- worldwide multicenter, randomized, double-blind, placebo-controlled ph III trial
- expected N=10,000 screened -> N=2270 patients randomized
- primary endpoint: disease-free survival

Dec 2011: end of recruitment

Prospective validation of biomarker = co-primary endpoint

Setting | Phase 3
---|---
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Loc. adv. stage Post chemorad | Tecemotide (L-BLP25) START target 1300 reported ASCO 13
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rEGF target 1000 ongoing
TG4010 TIME target 1000 ongoing
Racotumomab (1E10) target 1082 Ongoing
Lung cancer vaccination > antigen: MUC1 protein

- Overexpressed by most cancers including NSCLC
- Loss of polarity of expression: entire cell surface
- N-terminal ectodomain aberrantly glycosylated
- high MUC1 levels associated with poor prognosis *

[Diagram of mucin expression]


Lung cancer vaccination > compound: tecemotide (L-BLP-25)

- Antigen: tandem repeat peptide of MUC1

  **STAPPANHTASPDPASPAPPSTAP**-Lys

  25 aa lipopeptide (BLP-25)

- Adjuvant
  - monophosphoryl lipid A
  - in liposomal formulation

- Administration
  - s.c. / qw x8 -> q6w until PD
Lung cancer vaccination > ph3: tecemotide START trial

Stage III
- disease control after chemoradiotherapy (concurr. or sequential)
- no brain mets
- no immune disease

Tecemotide 1000 µg s.c.
qw (x8) -> q6w + BSC

Placebo same schedule + BSC

Primary endpoint: overall survival
Other endpoints: safety, TTP, symptoms

Stratified stage: IIA vs. IIIB
response: SD vs. OR
RT: concurrent vs. sequential region

Butts et al, ASCO 2013

Primary endpoint: Overall survival

<table>
<thead>
<tr>
<th></th>
<th>L-BLP25 (N=829)</th>
<th>Placebo (N=410)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median OS</td>
<td>25.6 mo</td>
<td>22.3 mo</td>
</tr>
<tr>
<td>Adjusted HR</td>
<td>0.88 (95% CI 0.75–1.03)</td>
<td>p=0.123*</td>
</tr>
<tr>
<td>Median follow-up</td>
<td>39.9 mo</td>
<td>37.7 mo</td>
</tr>
</tbody>
</table>

At risk (N)
Placebo: 410 353 285 188 127 108 88 69 33 18 4 0
L-BLP25: 829 757 617 429 301 255 204 128 73 33 8 0

*Two-sided, strata and multiplicity adjusted
OS: Subgroup analyses by randomization strata

<table>
<thead>
<tr>
<th></th>
<th>Median OS (months)</th>
<th>HR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage</strong></td>
<td>L-BLP25 vs. Placebo</td>
<td></td>
</tr>
<tr>
<td>Stage IIIA (N=487)</td>
<td>27.6 vs. 23.1</td>
<td>0.86 (0.67, 1.11)</td>
</tr>
<tr>
<td>Stage IIIB (N=752)</td>
<td>23.7 vs. 20.9</td>
<td>0.90 (0.74, 1.09)</td>
</tr>
<tr>
<td><strong>Region</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NA and Aus. (N=321)</td>
<td>34.1 vs. 21.7</td>
<td>0.79 (0.58, 1.09)</td>
</tr>
<tr>
<td>W. Europe (N=475)</td>
<td>24.2 vs. 22.3</td>
<td>0.91 (0.71, 1.17)</td>
</tr>
<tr>
<td>Rest of world (N=443)</td>
<td>21.8 vs. 22.7</td>
<td>0.95 (0.73, 1.22)</td>
</tr>
<tr>
<td><strong>Response to chemo/RT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable disease (N=396)</td>
<td>20.4 vs. 17.8</td>
<td>0.85 (0.65, 1.11)</td>
</tr>
<tr>
<td>Obj. response (N=843)</td>
<td>27.8 vs. 23.9</td>
<td>0.91 (0.75, 1.10)</td>
</tr>
<tr>
<td><strong>Chemo/RT type</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concurrent (N=806)</td>
<td>30.8 vs. 20.6</td>
<td>0.78 (0.64, 0.96)</td>
</tr>
<tr>
<td>Sequential (N=433)</td>
<td>19.4 vs. 24.6</td>
<td>1.11 (0.86, 1.43)</td>
</tr>
</tbody>
</table>

*Not adjusted for strata

Overall survival: Concurrent chemo/RT

- L-BLP25 (N=538)
- Placebo (N=288)

- Median OS: 30.8 mo vs. 20.6 mo
- Hazard ratio: 0.78 (95% CI 0.64–0.95), p=0.016

*Two-sided, adjusted for strata
## Lung cancer vaccination

### ph3: tecemotide safety

<table>
<thead>
<tr>
<th>Injection site reactions</th>
<th>L-BLP25 (N=1,024)</th>
<th>Placebo (N=477)</th>
<th>Grade 3/4 AE preferred term</th>
<th>L-BLP25 N=1,024 n (%)</th>
<th>Placebo N=477 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>176 (17.3)</td>
<td>56 (11.9)</td>
<td>Adrenal insufficiency</td>
<td>1 (0.1)</td>
<td>0</td>
</tr>
<tr>
<td>Any Grade 3/4</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>Guillain-Barre syndrome</td>
<td>1 (0.1)</td>
<td>0</td>
</tr>
<tr>
<td>Flu-like symptoms</td>
<td>L-BLP25 (N=1,024)</td>
<td>Placebo (N=477)</td>
<td>Hemolytic anemia</td>
<td>0</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Any</td>
<td>391 (38.2)</td>
<td>158 (33.1)</td>
<td>Temporal arteritis</td>
<td>0</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Any Grade 3/4</td>
<td>16 (1.5)</td>
<td>8 (1.7)</td>
<td>Any Grade 3/4</td>
<td>2 (0.2)</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>Cough</td>
<td>338 (33.0)</td>
<td>133 (27.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>238 (23.2)</td>
<td>112 (23.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Excellent safety: mostly grade 1-2 local or flu-like reactions
- No increase in severe immune-related AEs
- No increase in (symptoms of) RT pneumonitis

Butts et al, ASCO 2013

### biomarker? START exploratory analysis

- Analysis of plasma samples
- HLA type

<table>
<thead>
<tr>
<th>HLA subgroup</th>
<th>N</th>
<th>Overall survival (months) (Tecemotide vs Placebo)</th>
<th>Hazard ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary analysis population (mITT)</td>
<td>1239</td>
<td>25.6</td>
<td>22.3</td>
<td>0.88</td>
</tr>
<tr>
<td>HLA-A02 positive</td>
<td>586</td>
<td>25.8</td>
<td>22.7</td>
<td>0.89</td>
</tr>
<tr>
<td>HLA-DRB4 positive</td>
<td>557</td>
<td>28.0</td>
<td>22.3</td>
<td>0.85</td>
</tr>
<tr>
<td>HLA-B08 negative</td>
<td>976</td>
<td>26.3</td>
<td>22.8</td>
<td>0.51</td>
</tr>
</tbody>
</table>

Mitchell et al, WCLC 2013
**Lung cancer vaccination**

> biomarker? START exploratory analysis

<table>
<thead>
<tr>
<th>mITT</th>
<th>All subjects (n=1239)</th>
<th>25.6 vs. 22.3</th>
<th>0.89 (0.76, 1.04)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negative ([1:1.00]) (n=1085)</td>
<td>23.3 vs. 22.7</td>
<td>0.98 (0.85, 1.17)</td>
</tr>
<tr>
<td></td>
<td>Positive ([1:1.00]) (n=128)</td>
<td>43.2 vs. 17.0</td>
<td>0.41 (0.25, 0.69)</td>
</tr>
<tr>
<td></td>
<td>&lt; LLN (n=772)</td>
<td>23.1 vs. 21.7</td>
<td>0.96 (0.79, 1.16)</td>
</tr>
</tbody>
</table>

**Lung cancer immunotherapy**

- Introduction: immunotherapy
- Lung cancer vaccination
- Lung cancer immunomodulation
- Conclusion
Lung cancer immunomodulation

- “Disappointing historical experience”: levamisole, BCG, IL, IFN, C. parvum, thymosin,…

- PF-3512676 (Promune): TLR stimulation – **NEGATIVE**

- Talactoferrin alpha: gut-associated lymphoid tissue - **NEGATIVE**

- Ipilimumab (anti-CTLA4 MAb)

- Anti-PD1 and anti-PD-L1 MAb

Lung cancer immunomodulation > priming and effector phase

Lung cancer immunomodulation > compound: ipilimumab

- Human MAb inhibiting cytotoxic T lymphocyte antigen 4 (CTLA-4)
- promotes signaling to CD28 and stimulation of T cell response (priming phase)
- may block suppressive signal from regulatory T cells, and promote autoimmunity


Lung cancer immunomodulation > ph2: ipilimumab

- Primary endpoint: immune-related PFS

Lung cancer immunomodulation > ph2: ipilimumab safety

- Safety
  - "generally well tolerated"
  - grade 3-4 immune-related AEs
    - 15% phased ipilimumab / 20% concurrent ipilimumab / 6% control

- Similar to major toxicity in melanoma study *
  - colitis: besides corticosteroids, 4 pts received infliximab (anti-TNF) for diarrhea / colitis grade 3+; residual colitis in 4 pts
  - residual endocrine AEs requiring hormone-replacement in 8 pts
  - 14 deaths related to the study drugs, 7 to immune-related AEs


Lung cancer immunomodulation > ph2: ipilimumab efficicay

- irPFS
  - phased HR 0.72 – P=0.05
  - concurrent HR 0.81 – P=0.13

- OS
  - phased HR 0.87 – P=0.23
  - concurrent HR 0.99 – P=0.48

### Lung cancer immunomodulation > ipilimumab development

<table>
<thead>
<tr>
<th>Trial</th>
<th>Treatment arms</th>
<th>N&lt;sub&gt;rand&lt;/sub&gt;</th>
<th>Study population</th>
<th>Primary endpoint</th>
<th>Other endpoints</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase III randomised placebo-controlled NCT01285609</td>
<td>Carbo-paclitaxel + phased ipilimumab or placebo -&gt; maintenance ipilimumab or placebo</td>
<td>920</td>
<td>Stage IV or recurrent squamous NSCLC</td>
<td>OS</td>
<td>WHO-modified PFS, ORR</td>
</tr>
<tr>
<td>Phase III randomised placebo-controlled NCT01450761</td>
<td>Platinum-etoposide + phased ipilimumab or placebo -&gt; maintenance ipilimumab or placebo</td>
<td>1100</td>
<td>Advanced SCLC</td>
<td>OS</td>
<td>Immune-related PFS, WHO-modified PFS, ORR, duration of response</td>
</tr>
<tr>
<td>Planned ETOP phase II randomised placebo-controlled</td>
<td>Concurrent chemotherapy -&gt; maintenance ipilimumab or placebo</td>
<td>260</td>
<td>Stage I-III SCLC</td>
<td>OS</td>
<td>PFS, RECIST response, time-to-relapse, toxicity, translational research</td>
</tr>
</tbody>
</table>

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### Lung cancer immunomodulation > compounds: anti-PD-1 / anti-PD-L1

- Human MAb blocking programmed death 1 (PD-1) inhibitory receptor on activated T-cells or its ligand
- promotes attack of tumour cells by activated T cells (effector phase)
- may block function of regulatory T cells, and promote autoimmunity

"The race for the antibody"
- anti-PD-1: BMS-936558/Nivolumab, CT-011, MK-3475
- anti-PD-L1: BMS-936559, MedI-4736, MDPL-3280A
Lung cancer immunomodulation
> *compounds*: anti-PD-1 / anti-PD-L1

- **BMS-936558** (Nivolumab): human IgG4 anti-PD-1 (BMS)
  - at least 1 prior treatment (54% ≥3 prior treatments)
  - response rate (all pts): 17%
  - median duration of response: 74 wks

- **MPDL3280A**: human IgG1 anti-PD-L1 (Genentech)
  - at least 1 prior treatment (55% ≥3 prior treatments)
  - response rate (all pts): 23%
  - median duration of response: >45 wks (ongoing, median NR)

- **MK-3475**: humanized IgG4 anti-PD-1 (Merck MSD)
  - 2 prior treatments
  - response rate (all pts): 24%
  - median duration of response: >60 wks (ongoing, median NR)

---

Cancer immunomodulation
> *large ph1*: anti-PD-1

Day 1 15 29 43 57
* dose administered i.v. q2w

- **8 week treatment cycle**
- Rapid PD or clinical PD
- Unacceptable toxicity

- Off study
- FU every 8w x6 (48 wks)

- CR/PR/SD or PD - clinically stable

- Treat to confirmed CR, worsening PD, unacceptable toxicity, up to 12 cycles

**Patients**
- Heavily pretreated advanced melanoma, RCC, NSCLC, CRPC, CRC (PD after 1–5 systemic therapies)
- Some melanoma/RCC patients had prior immunotherapy (64% - 59%)

Lung cancer immunomodulation

> large ph1: anti-PD-1

<table>
<thead>
<tr>
<th>Anti-PD1</th>
<th></th>
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<tbody>
<tr>
<td>All therapy related AEs</td>
<td>70%</td>
</tr>
<tr>
<td>G3/4 therapy related AEs</td>
<td>14%</td>
</tr>
<tr>
<td>pulmonary</td>
<td>1%</td>
</tr>
<tr>
<td>diarrhea</td>
<td>1%</td>
</tr>
<tr>
<td>auto-immune*</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Discontinued for related AE</td>
<td>5%</td>
</tr>
<tr>
<td>Grade 5 (pulmonary)</td>
<td>N=3</td>
</tr>
</tbody>
</table>

* colitis, hepatitis, hypophysitis, thyroiditis


Brahmer et al, ASCO 2013 and WCLC 2013 update
Lung cancer immunomodulation > biomarker? PD-L1 IHC

- For all
  - PD-L1 expression appears to be strongly correlated with response rate
  - but long-lasting responses also seen PD-L1 negative tumours
  - responses regardless of histology, smoking, EGFR/KRAS mutation status

Horn et al, WCLC 2013 update

Lung cancer immunomodulation > PD-1 PD-L1 development

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<th>Trial</th>
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<th>Study population</th>
<th>Primary endpoint</th>
<th>Other endpoints</th>
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</thead>
<tbody>
<tr>
<td>Phase III randomised open label CheckMate017 NCT01642004</td>
<td>Nivolumab vs. docetaxel</td>
<td>264</td>
<td>Squamous cell NSCLC recurrent or progressing during/after platinum-based chemotherapy for stage IIIB/IV</td>
<td>ORR, OS</td>
<td>PFS, clinical benefit, duration of OR, time to OR</td>
</tr>
<tr>
<td>Phase III randomised open label CheckMate057 NCT01673867</td>
<td>Nivolumab vs. docetaxel</td>
<td>574</td>
<td>Non-squamous cell NSCLC recurrent or progressing during/after platinum-based chemotherapy for stage IIIB/IV</td>
<td>OS</td>
<td>ORR, PFS, clinical benefit</td>
</tr>
<tr>
<td>Phase II/III randomised open label POPLAR NCT01903993</td>
<td>MPDL3280A vs. docetaxel</td>
<td>180</td>
<td>Advanced recurrent NSCLC with FFPE specimen for PD-L1 staining</td>
<td>OS</td>
<td>ORR, PFS, safety, patient reported outcomes</td>
</tr>
<tr>
<td>Phase II/III randomised open label NCT01905657</td>
<td>MK-3475 low vs. MK-3475 high vs. docetaxel</td>
<td>920</td>
<td>Squamous cell NSCLC progressing after platinum-containing chemotherapy</td>
<td>OS</td>
<td>PFS, safety, ORR, response duration</td>
</tr>
</tbody>
</table>
Lung cancer immunotherapy

- **Introduction: immunotherapy**
- **Lung cancer vaccination**
- **Lung cancer immunomodulation**
- **Conclusion**

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Lung cancer immunotherapy

> conclusion

- **Lung cancer**
  - Strong immunosuppressive environment
  - Historical results (non-specific agents) disappointing
- **Recent cancer vaccination studies**
  - Better defined antigens and adjuvants
  - Low toxicity defines a unique treatment opportunity
  - Strong ph3 data from recent study with BLP-25
- **Recent cancer immunomodulation studies**
  - Better understanding of dendritic cell biology
  - Important toxicity may occur in some patients
  - Strong ph1 data with anti-PD-1/PD-L1
Thank you for your kind attention

Leuven, Gothic Town Hall (1448)