How to win in the evolving early-stage NSCLC landscape

Strategic considerations to successfully adapt to the rapidly changing Non-Small Cell Lung Cancer (NSCLC) global market following the introduction of checkpoint inhibitors in resectable disease (non-driver)

- Featuring referenced insights (2022) from CancerMPact® syndicated solutions
  - Patient Metrics
  - Treatment Architecture
  - Future Trends & Insights
  - Cancer Landscape
Following the clinical and commercial success of the anti-PD-(L)1 class in the unresectable and metastatic settings, immunotherapy (IO) is moving to early-stage disease with the aim of improving resectability and reducing post-surgical recurrence.

Checkpoint inhibitors (CPI) seek new horizons in resectable NSCLC (non-driver)

Adoption in the resectable setting will be high due to high unmet need for better treatments.
Limited differentiation
There are multiple studies investigating the same treatment intervention approach

Crowded competitive landscape
Many studies investigating same-class anti-PD-(L)1 drugs are expected to read out within the next three years.²,³

First global approvals highlight the risk of label restrictions
The risk of label restrictions by PD-L1 expression open the opportunity for differentiation across products and settings

Regional differences in label restrictions for anti-PD-(L)1 in NSCLC.²,³

<table>
<thead>
<tr>
<th>Stage IV metastatic</th>
<th>Stage III unresectable</th>
<th>Adjacent</th>
<th>Neoadjuvant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keytruda (1L)</td>
<td>Imfinzi (consolidation)</td>
<td>Tecentriq</td>
<td>Opdivo + chemo</td>
</tr>
<tr>
<td>≥ 1%</td>
<td>All comers</td>
<td>≥ 1%</td>
<td>All comers</td>
</tr>
<tr>
<td>≥ 1%</td>
<td>All comers</td>
<td>≥ 1%</td>
<td>To be determined</td>
</tr>
<tr>
<td>≥ 50%</td>
<td>≥ 1%</td>
<td>≥ 50%</td>
<td>To be determined</td>
</tr>
</tbody>
</table>

Primary completion date

Intervention Study 2021 2022 2023 2024 2025 2026
Neoadjuvant
Opdivo + chemo
Chemo ± radiotherapy (optional)
CheckMate-816
Peri-operative
Opdivo + chemo
Opdivo
CheckMate-77T
Keytruda + chemo
Keytruda
KEYNOTE 671
Imfinzi + chemo
Imfinzi
AEGEAN
Tecentriq + chemo
Tecentriq
IMpower130
Adjuvant
- Chemo + Tecentriq
Imfinzi
PEARLS/KEYNOTE 091
- ≥ 1 Chemo + Keytruda
Opdivo
IMpower101
- ≥ 1 Chemo + Opdivo
ANVIL
- ≥ 1 Chemo + Imfinzi
BR31

Data available Approval by geography Regulatory decision target date
Market size
CPI seeking new horizons in resectable disease

All analysis are current as of October 25, 2022
The key to winning resectable NSCLC

Understanding the global challenges and opportunities with a smaller market size than metastatic disease

The market size (treated patients) for resectable disease is significantly smaller than for metastatic disease

Global differences in management of resectable disease

In clinical practice, the standard of care management of resectable disease may vary across regions and pose different opportunities for each particular approach

Clinical and commercial profile of interventions in resectable disease

The differentiated clinical and commercial profile of each approach has strategic implications that may be leveraged in each market

Data derived from CancerMPact® modules:
1 Patient Metrics (2022)
2 Treatment Architecture (2022)

Success factors

Market Size

Potential increase of resectability and achievability of negative margins
Pathological surrogates (e.g., pathologic complete response [pCR], major pathological response [mPR]) of survival may enable innovative pay-per-performance
Risk of disease progression or developing adverse events after neoadjuvant therapy that can delay/prevent subsequent surgery
Cost of therapeutic intervention, including drugs and disease management, to payers
Ability to incorporate in clinical practice based on current disease management frameworks

Cost to payers

Risk of surgery delay
Pathological surrogates (e.g., pathologic complete response [pCR], major pathological response [mPR]) of survival may enable innovative pay-per-performance
Presence of original tumor biomass may allow a more efficient priming of immune cells and treat micrometastasis earlier
Potential increase of resectability and achievability of negative margins

Tumor immunological priming
Tumor downstaging and downsizing
Biological assessment

Positive differentiator (driver)
Neutral differentiator
Negative differentiator (barrier)

Neoadjuvant
Peri-operative
Adjuvant

All analysis are current as of October 25, 2022
Critical factors of commercial success

Regulatory restrictions, timing of market entry, brand identity, and product differentiation will determine uptake

**TIMING OF MARKET ENTRY**
With limited product differentiation, first approvals may gain strategic advantage in a historically “first-come first-serve” market

**BRAND IDENTITY**
Leveraging halo-effect of IO leaders in unresectable or metastatic NSCLC

**REGULATORY RESTRICTIONS**
Understanding impact of and seizing opportunities created by regulatory label restrictions

**SECURING REIMBURSEMENT**
Leveraging surrogate survival endpoints (e.g., pathological complete response (PCR), major pathological response (MPR)) may enable pay-per-performance models

**STRENGTH OF CLINICAL DATA**
Generating evidence in clinical studies and subgroup analyses will be key to position products and approaches in resectable disease

**PRODUCT DIFFERENTIATORS**
Leveraging product differentiation (e.g., favorable dosing schedules) and innovation (e.g., subcutaneous/ oral formulation) may foster stakeholder preference and drive uptake

**IDENTIFYING AT-RISK POPULATION**
Exploring biomarker approaches (e.g., minimal residual disease (MRD), circulating tumor DNA (ctDNA)) that may guide treatment decisions post-surgery, hence enabling ways to justify reimbursement

**UNDERSTANDING MARKET & PRACTICE DYNAMICS**
Analyzing drivers and barriers that can influence uptake of each product and approach in each region

### Adapting to an evolving clinical landscape

Fostered by the introduction of IO in resectable disease, understanding how IO naïve and IO progressors fit within a new treatment paradigm that enables exposure to IO agents in resectable disease will be key to seizing opportunities in an evolving clinical landscape

**Pipeline products for IO naïve resectable NSCLC**
Exploring next-generation IO products that synergize with anti-PD-(L)1 agents in resectable disease in IO naïve patients

**Pipeline products for IO progressors**
Understanding how approaches currently investigated only in refractory metastatic NSCLC in IO progressors may have an opportunity in earlier lines of therapy (e.g., 1L)

**New studies in 1L metastatic NSCLC**
Including a representative sample of IO-exposed patients in new studies for 1L, as IO may become standard of care in resectable disease

**Marketed products**
Adapting to shifts in SOC that occur earlier in the treatment paradigm by generating RWE in IO progressors across different lines of therapy

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All analysis are current as of October 25, 2022

Key for winning in resectable NSCLC

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All analysis are current as of October 24, 2022
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