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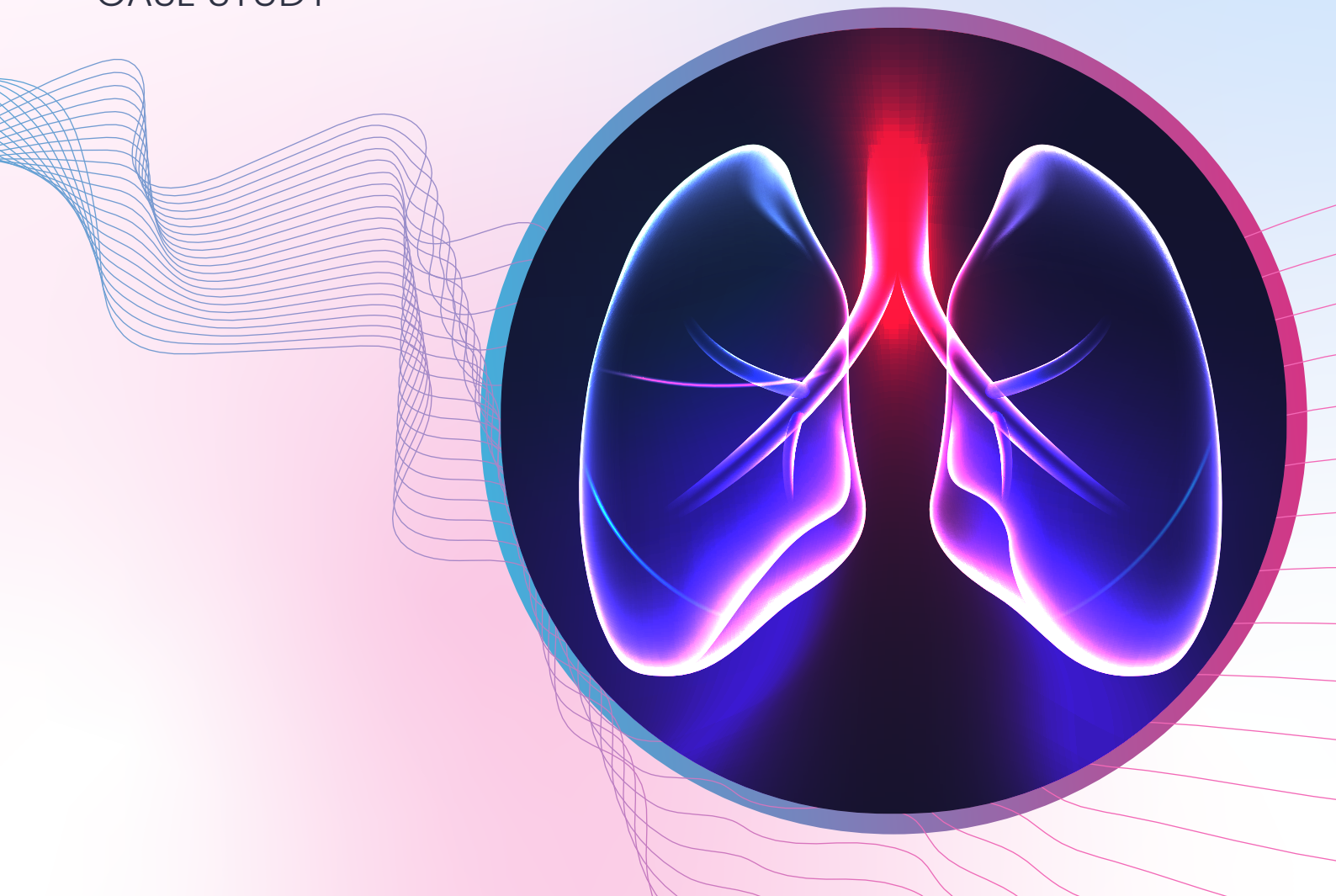
Landscape survey of non-small-cell lung carcinoma (NSCLC) for immuno-oncology (IO)

Comprehensive data helped the client select relevant biomarkers, develop a greater understanding of the mechanism of immune response, and identify alterations in immune cell/TIL profiles in different lines of therapy

CASE STUDY



Client

Industry
Large pharma

Services used
Bioinformatics, disease landscape reports, data curation, biomarker discovery, and clinical trials outcomes data

Specification

Our client is a large pharmaceutical company based in the United States. One of its research teams is seeking potential new treatments for non-small-cell lung cancer and is engaged in identifying appropriate biomarkers to help design effective clinical trials. The identification process would require a thorough survey and analysis of existing NSCLC clinical trial data. The data would need to be extracted from a wide library of literature and consistently structured before analysis. This process demands significant time and resources, so the client engaged Excelra to execute the survey, extract the data, and deliver a comprehensive analysis.

Our approach

The client asked us for a detailed report on clinical studies with checkpoint inhibitors for NSCLC that target PD-L1 or PD-1. The report also needed to include a detailed review of the inhibitors' potential benefits within four different lines of therapy: naïve patients, first-line therapy, second-line therapy, and third-line therapy

To meet the client's requirements, we developed a text-mining algorithm to identify relevant literature. Once the algorithm had delivered an exhaustive list, our scientists manually curated, annotated, and analyzed the information, delivering a refined list to the client.

Our curation exercise captured information from four focus areas:

1. Immunotherapies NSCLC clinical studies

Our qualified subject matter experts curated 82 relevant studies and assessed them for several efficacy-related data points:

- Line of therapy
- Circulating immune cell profile
- TILs profile
- Correlation of clinical response and baseline immune profile
- Correlation of clinical response and baseline TILs
- Correlation of baseline PD-L1 status with TILs or peripheral immune cells
- Correlation of clinical response and TPS for PD-L1 expression
- Baseline mutation and clinical activity
- PD-L1 expression assay

To produce the immunotherapies and clinical study landscape, our experts followed a consistent, proven workflow:

1 Input data

The input data was obtained using a lexicon built for NSCLC

2 Identification of published clinical studies for NSCLC

The initial curation exercise was executed using text-mining algorithms. We targeted published clinical studies for NSCLC.

3 Annotation of identified studies

Our experts annotated clinical studies associated with NSCLC with reference to the line of treatment, tumor, stage, and histology.

4 Data collection and preparation for analysis

They then completed further manual annotation of data from articles for immune profile, TILs, mutation status, tumor proportion score, markers (CD226 axis), differentially-expressed genes, and PD-L1 tests.

5 Data analysis and results

Finally, we performed a correlation analysis to identify trends in the data.

The compiled NSCLC landscape included details of drugs, lines of therapies, and efficacy-related data points (Fig.1)

Drug name	Pembrolizumab (23 studies)				
Line of therapy	Naïve patients	First line	Second line	Third line	Mixed
Circulating immune cell profile	—	YES (1)	YES (1)	YES (1)	YES (4)
TILs profile	YES (1)	—	—	—	YES (1)
Correlation of clinical response and baseline immune profile	—	—	—	YES (1)	YES (1)
Correlation of clinical response and baseline TILs	—	—	—	—	YES (3)
Correlation of baseline PD-L1 status with TILs or peripheral immune cells	—	—	—	—	YES (1)
Correlation of clinical response and TPS for PD-L1 expression	—	—	YES (1)	YES (3)	YES (7)
Baseline mutation and clinical activity	—	YES (1)	—	YES (1)	YES (1)
PD-L1 expression	—	YES (1)	YES (4)	YES (6)	YES (7)

Figure 1: Summary of the compiled NSCLC landscape for pembrolizumab

Across NSCLC clinical studies, IO drugs are tested as monotherapy or in combination with chemotherapy, radiation, small molecules, and other immunotherapies at different stages of disease and lines of treatment. Table 1 summarizes the curated information for three treatment regimes:

Treatment regimen	IO Mono (52 studies)	IO + Chemo (7 studies)	IO + Radiation (2 studies)
Circulating immune cell profile	YES (7)	–	YES (1)
TILs profile	YES (3)	–	–
Correlation of clinical response and baseline immune profile	YES (2)	–	–
Correlation of clinical response and baseline TILs	YES (2)	–	–
Correlation of baseline PD-L1 status with TILs or peripheral immune cells	Yes (1)	–	–
Correlation of clinical response and TPS for PD-L1 expression	YES (38)	YES (4)	YES (1)
Base line mutation and clinical activity	YES (1)	–	YES (1)
PD-L1 expression	YES (45)	YES (1)	YES (1)

Table: Treatment regimen for NSCLC and the measured clinical response

2. Comparative analysis of anti-PD-1 and anti-PD-L1 treatment and efficacy endpoints

A comparative analysis of anti-PD-1 and anti-PD-L1 revealed that treatment and efficacy endpoints were consistent across both. However, the correlation of clinical response and baseline TILs, correlation of baseline PD-L1 satus with TILs or peripheral immune cells, and baseline mutation and clinical activity are unique to anti-PD-1 (Fig.2).

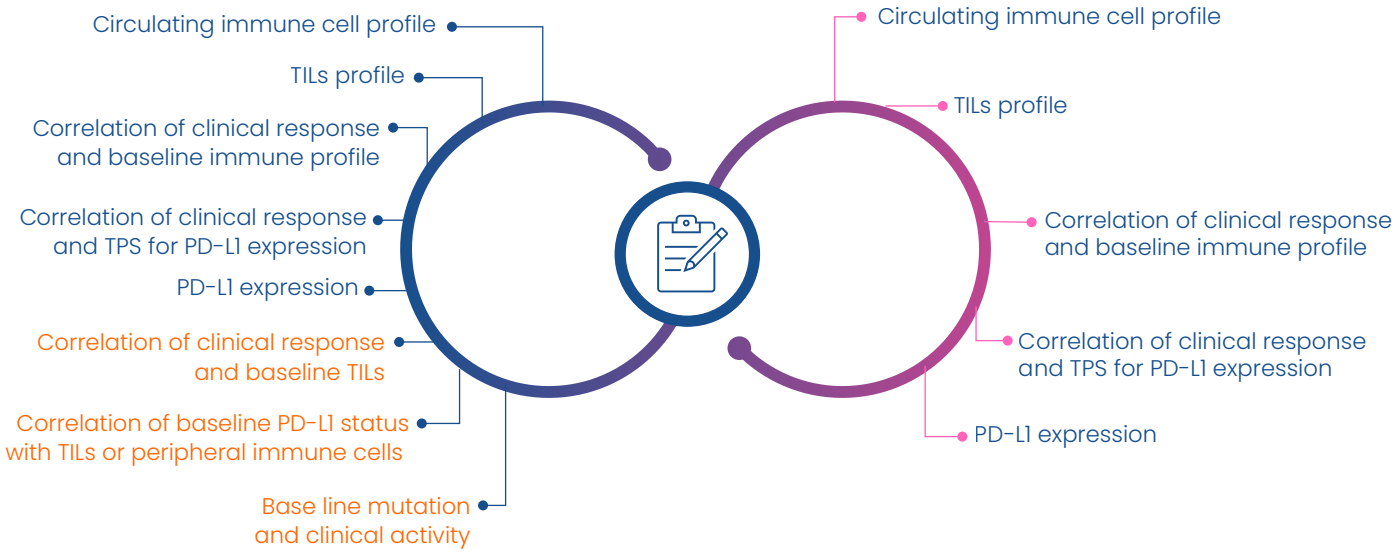


Figure 2: Anti-PD-1 and anti-PD-L1 treatment and efficacy data points. **Blue** data points are common for both anti-PD-1 and anti-PD-L1. **Orange** data points are unique to anti-PD-1

3. Treatment regimens in NSCLC across different lines of therapy and comparative analysis of efficacy endpoints

Non-small-cell lung cancer treatments have improved over the last two decades. There has been an increase in the number of active drugs, the development of effective regimens, and the introduction of salvage therapy after the failure of first-line treatment. The immunotherapy regimens currently being tested in the clinical studies and their efficacy endpoints are highlighted below

Naïve patients	• Nivolumab (2) • Nivolumab + Ipilimumab (1) • Pembrolizumab (1)
First-line therapy	• Atezolizumab (1) • Atezolizumab+Nab-paclitaxel+Carboplatin (2) • Atezolizumab+Bevacizumab+Carboplatin+Paclitaxel (1) • Atezolizumab+Carboplatin/Cisplatin+Pemetrexed (1) • Atezolizumab+Nab-paclitaxel/Carboplatin+Nab-paclitaxel/Carboplatin+ Pemetrexed/Carboplatin+Paclitaxel (1) • Durvalumab (1) • Durvalumab+Tremelimumab (1) • Durvalumab+Gefitinib (1) • Nivolumab+Ipilimumab (2) • Nivolumab+Ipilimumab+Carboplatin+Paclitaxel+Pemetrexed+Cisplatin (1) • Pembrolizumab/Pembrolizumab+Pemetrexed+Carboplatin+Paclitaxel (1) • Pembrolizumab+Quavonlimab (1) • Cemiplimab (1)
Second-line therapy	• Pembrolizumab (3) • Pembrolizumab+Azacitidine (1) • Pembrolizumab+Radiotherapy (1) • Nivolumab (9) • Nivolumab+ALT-803 (1) • Nivolumab+Ceritinib (1) • Atezolizumab (9) • Durvalumab (5) • Durvalumab+Ramucirumab (1) • Cemiplimab (1)
Third-line therapy	• Pembrolizumab (4) • Pembrolizumab+Ramucirumab (1) • Pembrolizumab+Entinostat (1) • Nivolumab (2) • Durvalumab (2) • Durvalumab+Tremelimumab (1)
Mixed therapy	• Nivolumab (1) • Nivolumab+Pegilodecakin (2) • Nivolumab+Cisplatin+Gemcitabine/Cisplatin+Pemetrexed/Carboplatin+ Paclitaxel+Bevacizumab/Docetaxel (1) • Pembrolizumab (6) • Pembrolizumab+Radiation therapy (1) • Pembrolizumab+Pegilodecakin (2) • Atezolizumab (4) • Durvalumab (2) • Durvalumab + Tremelimumab (3) • Durvalumab+Tremelimumab+Pemetrexed+Platinum/Etoposide+Platinum/ Gemcitabine+Platinum/Carboplatin+Nab-paclitaxel (1)

Figure 3: Immunotherapy regimen in NSCLC clinical studies

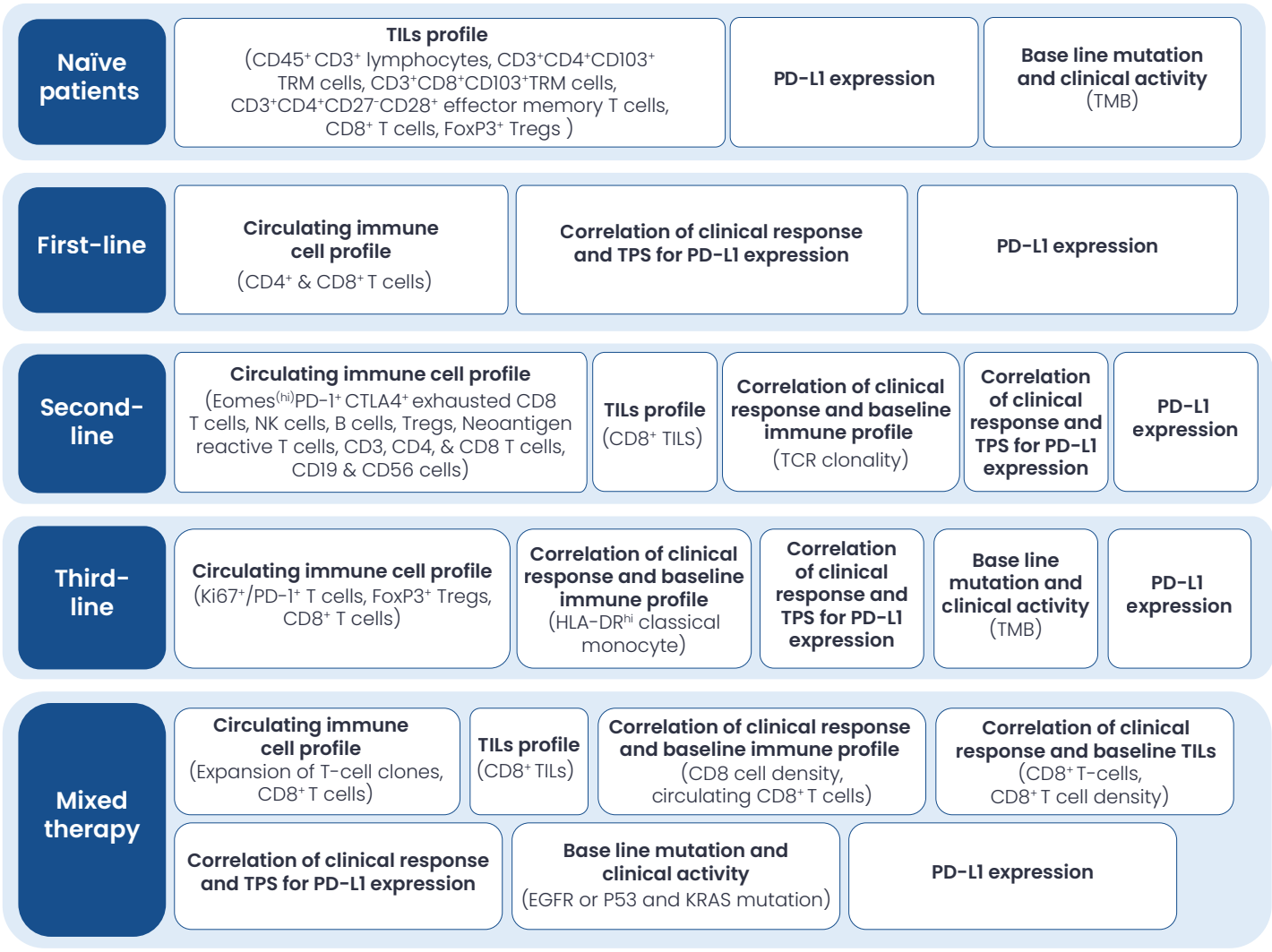


Figure 4: Comparative analysis of efficacy endpoints between different lines of therapy

4. PD-L1 Assays and correlation with clinical response

The studies documented multiple different assays for evaluating PD-L1 expression: PD-L1 IHC 22C3 pharmDx, PD-L1 IHC 28-8 pharmDx, IHC [Clone E1L3N], etc. We observed that the majority of PD-L1 tests are carried out with the PD-L1 IHC 22C3 pharmDx assay, and distinct PD-L1 assays are employed based on the line of therapy. We also noted several correlations between tumor proportion score (TPS) for PD-L1 expression and clinical response (Fig.5).

Figure 5: PD-L1 assays and association with the clinical response across different lines of therapy

The results

Our client required high-quality information, delivered quickly and according to precise specifications. With our outstanding data curation capabilities, we were able to assess the requirements and provide an exceptional NSCLC landscape survey to support the client's clinical trial strategy. We submitted a comprehensive data set that has helped the client select relevant biomarkers, develop a greater understanding of the mechanism of immune response, and identify alterations in immune cell/TIL profiles in different lines of therapy. Our high-quality, analysis-ready data has supported the client's clinical trial decisions and is contributing to its ongoing research.

If you're ready to benefit from our data curation and disease landscape surveys, **let us know**. Whatever your goal, we'll help you achieve it.

Our service portfolio

Data

Data curation
Filter out the noise, focus your attention

Clinical data
Analysis-ready data for informed clinical decision-making

Semantic data
Refine your decisions, find your value

Insights

Bioinformatics
Illuminate the path to faster discoveries

Data science
Unlock the power of data

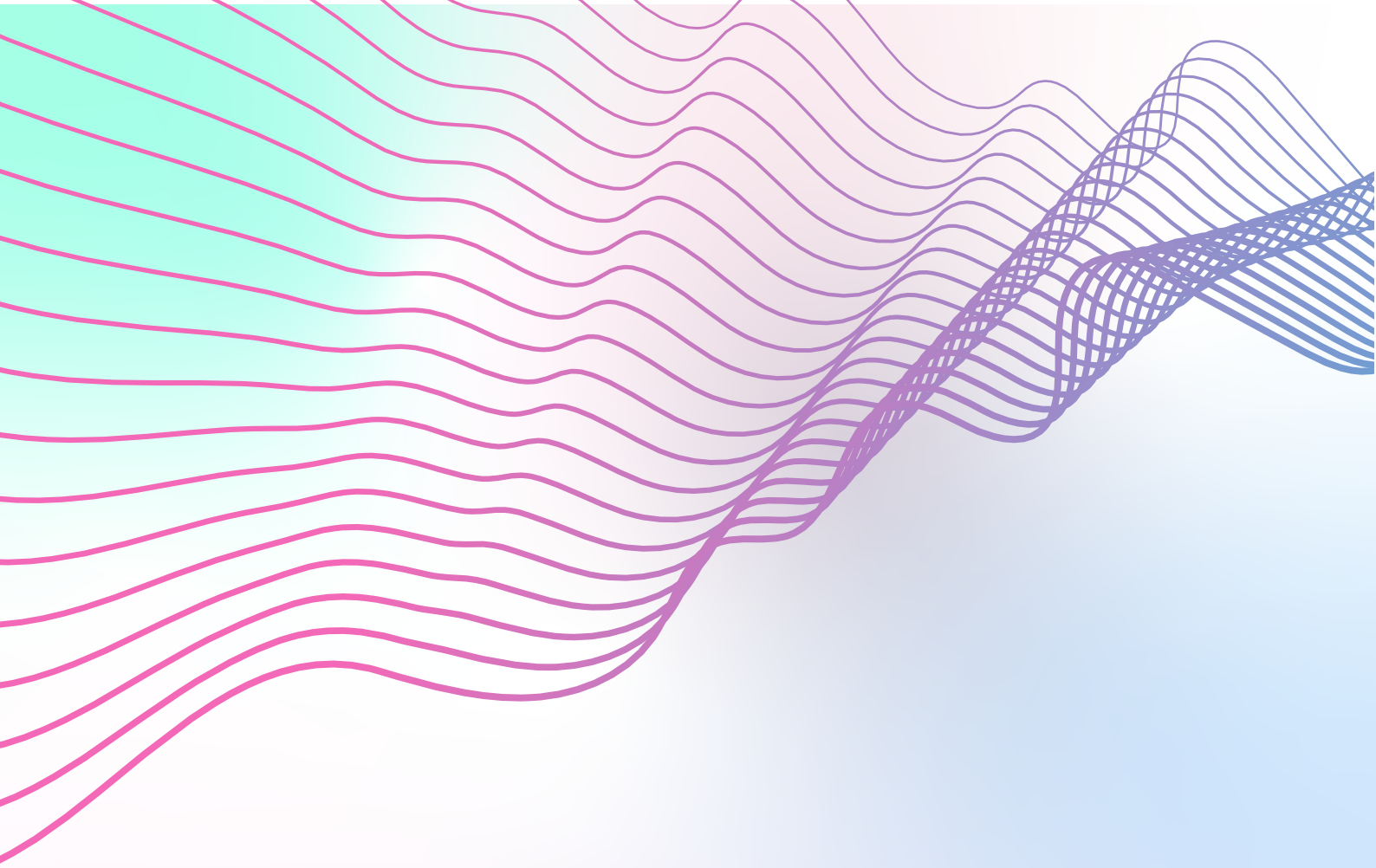
Visualization
Pictures paint a thousand words

R&D technology

Product design and development
Unlock your potential with data-driven design and development

Cloud enablement
Optimize your output on the cloud

Data engineering
Mitigate risks, protect your data, and rationalize your portfolio and processes.



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