Pipeline & Clinical Trials Intelligence Town Hall: How Do Editorial Policies Affect Content and Coverage?

2019 SLA Pharmaceutical And Health Technology Division (DPHT) Spring Meeting
April 14-16, 2019 / Hilton Penn's Landing / Philadelphia, PA

Moderator: Diane Webb, President, BizInt Solutions

Panelists:

Adis Insight (Springer): Glenn Whiteside, Editorial Product Specialist
Cortellis (Clarivate Analytics): Christopher Mundy, Director, Solutions Consulting (representing Anne LeCocq, Director, Business of Science)
Citeline (Informa Pharma Intelligence): Karen Currie, Executive Director, Editorial

Town Hall Report by Diane Webb and Matt Eberle, BizInt Solutions

Background

The Pipeline & Clinical Trials Intelligence Town Hall was held at the 2019 PHT Spring Meeting in Philadelphia, PA. Representatives from three of the leading pipeline and clinical trials databases — Clarivate Analytics, Citeline (Informa Pharma Intelligence), and AdisInsight (Springer) — offered insight into how their editorial policies affect search results and content.

Rather than establishing which "database is best", the goal was to provide insight into how the editorial policies at each company affect search results and database content.

The panel discussion included examples of similar searches across the three pipeline databases, with panelists providing explanations for discrepancies and differences in coverage and content. Panelists also discussed how clinical trial data is integrated with their pipeline data.

There was not enough time during the Town Hall to explore all the examples in detail, and the panelists agreed to provide their responses in writing for this report.

How the pipeline examples were created

In order to explore differences in coverage and content, we used an intentionally simple search for a single indication: mesothelioma. We conducted the following searches on April 4, 2019:

- Adis R&D Insight: Indication is Mesothelioma
- Cortellis: Indications & Therapy (Active Indications (Mesothelioma)) OR Indications & Therapy (Inactive Indications (Mesothelioma))
- Pharmaprojects: Drug Disease is Mesothelioma

The searches retrieved a total of 390 records — 104 from R&D Insight, 125 from Cortellis, and 161 from Pharmaprojects.

Search results each database were imported into BizInt Smart Charts Drug Development Suite and combined into a single report. The "Identify Common Drug Names" tool was used to identify which records from the three databases were related to the same drug, and 243 drugs were identified in the combined set.

50 of these 243 drugs were found in all three databases, but 42 drugs were found in the search results from only two databases, and 151 were retrieved from just one of the databases. This result is consistent with other case studies we have conducted and is due to differences in indication indexing (see Example 4).

To explore other differences in content, we identified differences in highest phase for the same drug (see Example 1) and variations in company information (see Examples 2 and 3).

These examples are based on searches performed on 4 April 2019 and do not reflect any subsequent updates to the records.

Many thanks to the members of the Adis, Cortellis and Citeline editorial teams who participated in the Town Hall and contributed remarks on the examples!

Example 1: Editorial policy for selecting Highest Phase

Below are two examples of mesothelioma drugs where the pipeline databases report different values for highest phase for the same drug. Please explain why your editorial team assigned the phases shown for the drugs below:

	Primary Drug Name	Common Drug Name	Database	Global Status	Latest Change Date
147	Ganetespib - Aldeyra Therapeutics	ganetespib	Adis R&D Insight	Phase II	2018-10-24
148	ganetespib	ganetespib	Citeline Pharmaprojects	Phase II Clinical Trial	2018-11-15
149	ganetespib	ganetespib	Cortellis from Clarivate Analytics	Phase 1 Clinical	2018-11-15

	Primary Drug Name	Common Drug Name	Database	Global Status	Latest Change Date
300	Ranpirnase	ranpirnase	Adis R&D Insight	Phase I/II	2017-08-11
301	ranpirnase	ranpirnase	Cortellis from Clarivate Analytics	Phase 2 Clinical	2018-12-25
302	ranpirnase	ranpirnase	Citeline Pharmaprojects	No Development Reported	2018-08-20

Response from **Adis** *editorial team*

Phase II was assigned to ganetespib (in Aug 2015) when a phase II study started in ovarian cancer. That information was presented in a company quarterly report, and in a ClinicalTrials.gov record. That trial is still recruiting patients hence the development 'line' is retained as active. In addition, there is a phase II trial underway in mesothelioma which is represented by a ClinicalTrials.gov record and on the Aldeyra pipeline (2019).

Ranpirnase was assigned a status of Phase I/II based on a trial in genital warts and HPV infections that completed towards the end of 2016. The company announced positive results from the trial in March 2017 hence development is considered to be active. The development line will be marked for review if no new development is found after 24-36 months. Company pipeline indicates active development for ranpirnase in Ebola, however the website is not up to date.

Response from **Cortellis** *editorial team*

Between the time the analysis was done and the panel, the phase was updated for both these drugs in Cortellis.

Response from **Citeline** *editorial team*

In Pharmaprojects, Global Status is the highest status achieved by the drug in any indication that is being pursued by a commercial entity. Ganetespib is in Phase II of development for mesothelioma and ovarian cancer. Trials described as "Phase I/II" are designated as Phase II in Pharmaprojects.

Sources reviewed by Pharmaprojects indicate that ranpirnase is no longer in development. The current website indicates the company is 'seeking partners' and 'results expected in 2015'. Pharmaprojects will assign this status to a drug when there appears to be no active development for 2+ years.

Thoughts from BizInt

In order to determine the highest phase of development, identifying the most advanced trial with the drug may not be the whole answer. Pharmaprojects specifically references the importance of development by a commercial entity. During the panel discussion, it become clear that even when all publishers had seen the same trial, they might disagree over whether there was a commercial entity associated with the trial.

Then there is the question of when to change the status of a drug to indicate no active development. Adis will make this determination if no active development is found after 2 to 3 years, while Pharmaprojects does the same if no development is seen after 2 years. But there is still an editorial decision to be made. Pharmaprojects appears to base the decision on statements found on a company website while Adis' decision hinges on announcement of trial results in 2017. Adis also referenced the company website, but notes that the website is out of date.

Example 2: Editorial policy for companies associated with a drug

Explain the differences in the company name selected for the different company fields.

Combined: 3 Databases_Mesothelioma 2019_04_04

	Primary Drug Name	Common Drug Name	Database	Originator	Licensee	Companies	Other Companies
23	**Amatuximab - Eisai**	amatuximab	Adis R&D Insight	National Cancer Institute (USA) (Originator)	Morphotek (Licensee)	National Cancer Institute (USA) (Originator) Morphotek (Licensee)	Eisai Co Ltd (Owner)
24	**amatuximab**	amatuximab	Cortellis from Clarivate Analytics	National Cancer Institute	Morphotek Inc	National Cancer Institute Morphotek Inc	
25	**amatuximab**	amatuximab	Citeline Pharmaprojects	Eisai		Eisai	

Response from **Adis** *editorial team*

In Adisinsight, the generic name of the drug is associated with the drug's owner and/or the key developer(s) of the programme. This is reflected in the drug name which is displayed at the top of the drug profile.

In the case of amatuximab, the drug originated from a development programme at the NCI and the IP was bought by Morphotek, which was acquired by Eisai as a subsidiary company. Hence the parent company Eisai owns both Morphotek and the IP for the drug.

An organisation that has an agreement with the owner to licence the rights to develop the drug in a certain region is assigned the role of licensee. If the license agreement is for marketing the drug then the market licensee role is assigned and the country where that license is valid is also assigned.

A collaborator is an organisation whose role is either described by the organisation as a collaborative agreement (where we can't pin it as a licensee) or no defined relationship is given by the organisation(s).

The originator of a drug programme never changes even if that organisation is a 'ceased' organisation or has no role in the development of the programme.

BizInt Smart Charts places the owner into a column entitled 'Other companies' but that's just the way the BizInt chart works. In Adisinsight, the organisation table depicts the roles of the organisations involved in developing the drug programme.

Response from **Cortellis** *editorial team*

Cortellis CI has the originator for Amatuximab as NCI and development by Morphotek (a subsidiary of Eisai). The drug is ultimately owned by Eisai, but Eisai is not specifically listed in the development history table. However, the link from Morphotek to Eisai is made in Cortellis in the company hierarchy. A company may not necessarily appear in the drug record if not playing any role in the development.

Response from **Citeline** *editorial team*

Pharmaprojects' coverage includes pipeline drugs which are being developed by commercial organizations; academic and/or government development work is not in scope. Eisai acquired amatuximab from Morphotek in 2004 and the drug is currently listed on Eisai's pipeline page and is in development for mesothelioma. Of note, the work undertaken by the NCI will be included in Trialtrove.

Thoughts from BizInt

When considering which organization names should be included in a drug record, the two key questions appear to be whether or not it is a commercial organization and the role the organization plays in active development of the drug. Based on the response from Pharmaprojects, only commercial organizations will be listed, while Adis and Cortellis will list non-commercial organizations, such as NCI, as the originator. Cortellis may not list a company in a drug record if the company has no active role in development, even though they are aware that the developing company is owned by a parent company.

Adis has a separate designation, Owner, for the parent company. BizInt Smart Charts offers the organization table from AdisInsight as a separate column called Organisations. AdisInsight also provides an Other Companies column, which includes organizations not listed as originators or licensees, with the role shown in parentheses after the organization name.

Example 3: How should one select the single "best" company for a drug?

Please discuss how you select the company names for each field, and how you would recommend the analyst "automatically" choose a single company name for analyses and visualizations.

	Primary Drug Name	Database	Originator	Licensee	Companies	Notes	Other Companies
49	**Belinostat - Onxeo**	Adis R&D Insight	TopoTarget (Originator)	Pint Pharma (Market Licensee) Spectrum Pharmaceuticals (Licensee) Servier (Sub-licensee)	TopoTarget (Originator) Pint Pharma (Market Licensee) Spectrum Pharmaceuticals (Licensee) Servier (Sub-licensee)	Belinostat, a small-molecule, hydroxamate-type inhibitor of class I, class II and class IV histone deacetylase (HDAC) enzymes, has been developed by Onxeo (formerly TopoTarget) and Spectrum Pharmaceuticals	Onxeo SA (Owner) CIMA- Universidad de Navarra (Collaborator) Clinigen (Collaborator) Emory University (Collaborator) Hospices Civils de Lyon (Collaborator) National Cancer Institute (USA) (Collaborator) Synovo (Collaborator)
50	**belinostat**	Citeline Pharmaprojects	TopoTarget	Spectrum Pharmaceuticals Servier Celldex Therapeutics Pint Pharma	TopoTarget Spectrum Pharmaceuticals Servier Celldex Therapeutics Pint Pharma	Onxeo has entered into an exclusive license agreement with Pint Pharma for the commercialization of belinostat. Under the terms of the agreement, Pint Pharma will register, commercialize, and promote belinostat in seven countries	
51	**belinostat (iv, cancer), Onxeo/Spectrum**	Cortellis from Clarivate Analytics	TopoTarget UK Ltd	Spectrum Pharmaceuticals Inc Pint Pharma Servier Canada Inc Onxeo SA	TopoTarget UK Ltd Spectrum Pharmaceuticals Inc Pint Pharma Servier Canada Inc Onxeo SA	Onxeo, following the merger of BioAlliance Pharma with TopoTarget (formerly Prolifix), with collaboration partner Spectrum, has developed and launched the injectable HDAC class I/II/IV inhibitor belinostat	

Response from **Adis** *editorial team*

To identify the main developer of a drug, Adis suggests the organization designated as Owner, Onxeo SA in the case of belinostat. Also, in the drug name we append the drug's owner and developer.

Response from **Cortellis** *editorial team*

The company name 'TopoTarget' applies to two companies. One was a UK company called Prolifix that was bought by Danish company TopoTarget in 2002 and renamed TopoTarget UK Ltd, but retained its identity as a UK subsidiary. The Danish TopoTarget merged with BioAlliance Pharma (now Onxeo SA) in 2014, taking the UK subsidiary with them. We have the UK company TopoTarget UK Ltd as the originator of belinostat (from WO-200230879). Pint, Servier and Spectrum came into the record via development and/or commercialization agreements (there are 15 deals associated with the record). To clarify further – the reason 'Servier Canada' rather than just 'Servier' was used is that they are specifically named in the agreement with Spectrum. The drug is named 'belinostat (iv, cancer), Onxeo/Spectrum' to distinguish it on our database from an oral formulation (which is at a much earlier stage of development). Onxeo/Spectrum are the two main developers of the drug.

Response from **Citeline** *editorial team*

The Originator, TopoTarget, is listed first in the cell containing the list of Companies. All others falling underneath it represent licensees.

Thoughts from BizInt

Identifying a single key company for a drug is a challenge for the analyst and editor alike. Clarivate identifies the complex history of belinostat, our example drug, and identifies two companies as the main developers of the drug, one of which is identified by Adis as the Owner company. Clarivate's Development Summary clearly indicates Oxneo as the main developer, but the Clarivate record only has three company fields: Originator, Active Companies, and Inactive Companies. Pharmaprojects identifies a single originator company and lists all others as licensees, including one, Spectrum, identified by Clarivate as a main developer.

Example 4: Editorial policy for indexing indications for drugs

In the combined chart, 42 drugs were retrieved by two databases, but not by the third. Please explain why your database did not index these drugs for mesothelioma:

	Primary Drug Name	Database	Drug Development Phase		
			Disease	Status	Country
1	BAY-2287411	Cortellis from Clarivate Analytics	Mesothelioma	Phase 1 Clinical	Europe, US
			Ovary tumor	Phase 1 Clinical	Europe, US
			Pancreatic ductal adenocarcinoma	Phase 1 Clinical	US, Europe
2	BAY-2287411	Citeline Pharmaprojects	Cancer, ovarian	Phase I Clinical Trial	
			Cancer, mesothelioma	Phase I Clinical Trial	
3	DS 1647	Adis R&D Insight	Glioblastoma	Phase II	Japan
			Mesothelioma	Phase I	Japan
			Prostate cancer	No development reported (I)	Japan
4	DS-1647	Cortellis from Clarivate Analytics	Glioma	Phase 2 Clinical	Japan
			Mesothelioma	Phase 1 Clinical	Japan
			Stomach tumor	Discovery	Japan

- ***Adis R&D Insight:*** *rebastinib, BAY-2287411*
- ***Clarivate Cortellis:*** *cediranib, sorafenib*
- ***Citeline Pharmaprojects:*** *DS-1647, dovitinib*

Response from **Adis** *editorial team*

Rebastinib is in a phase I/II trial for solid tumours. The phase II portion of the study is going to recruit patients with mesothelioma. We'll add the specific indications when that portion of the trial starts, or before the trial record is updated if there is other evidence pointing to development at the higher phase. Editorial policy is to index the broad indication, solid tumours in the case, at Phase and specific indications from Phase II onwards once the development focus is better defined. Company pipeline represents solid tumours (including several types).

BAY 2287411 is in a phase I study in patients with solid tumours expressing mesothelin. Trial inclusion criteria includes patients with various tumour types, including mesothelioma. Because this is a Phase I trial exploring essentially drug toxicity, we have indexed the broad term solid tumours. Company pipeline does the same.

Response from **Cortellis** *editorial team*

In both cases the mesothelioma indication is covered in trials run by NCI not by the originator or developing companies (cediranib – NCT00243074, and sorafenib – NCT00107432). If the company is not involved with a trial that is investigator-led, the indication should not be listed in the development status if the company does not list it as an active indication on its pipeline. If the company is involved with the investigator-led trial, the trial should be described in the drug record, but it should be made clear in the first paragraph and clinical data section that the trial is investigator-led with the company acting as a collaborator. However, in Cortellis you can find a small number of drug records in which, for example, NCI is indexed as the active company, but in these cases NCI is acting as the developer of the drug. Cortellis provided some further details on why they have mesothelioma indexed for the drugs discussed by Adis and Citeline.[1]

Response from **Citeline** *editorial team*

Dovitinib and DS-1647 were not indexed in Pharmaprojects for mesothelioma because the organization that has evaluated the drug in this indication is not an industry/commercial entity [Phase II, Ontario Clinical Oncology Group; Phase I, University of Tokyo]. Both trials are included in Trialtrove.

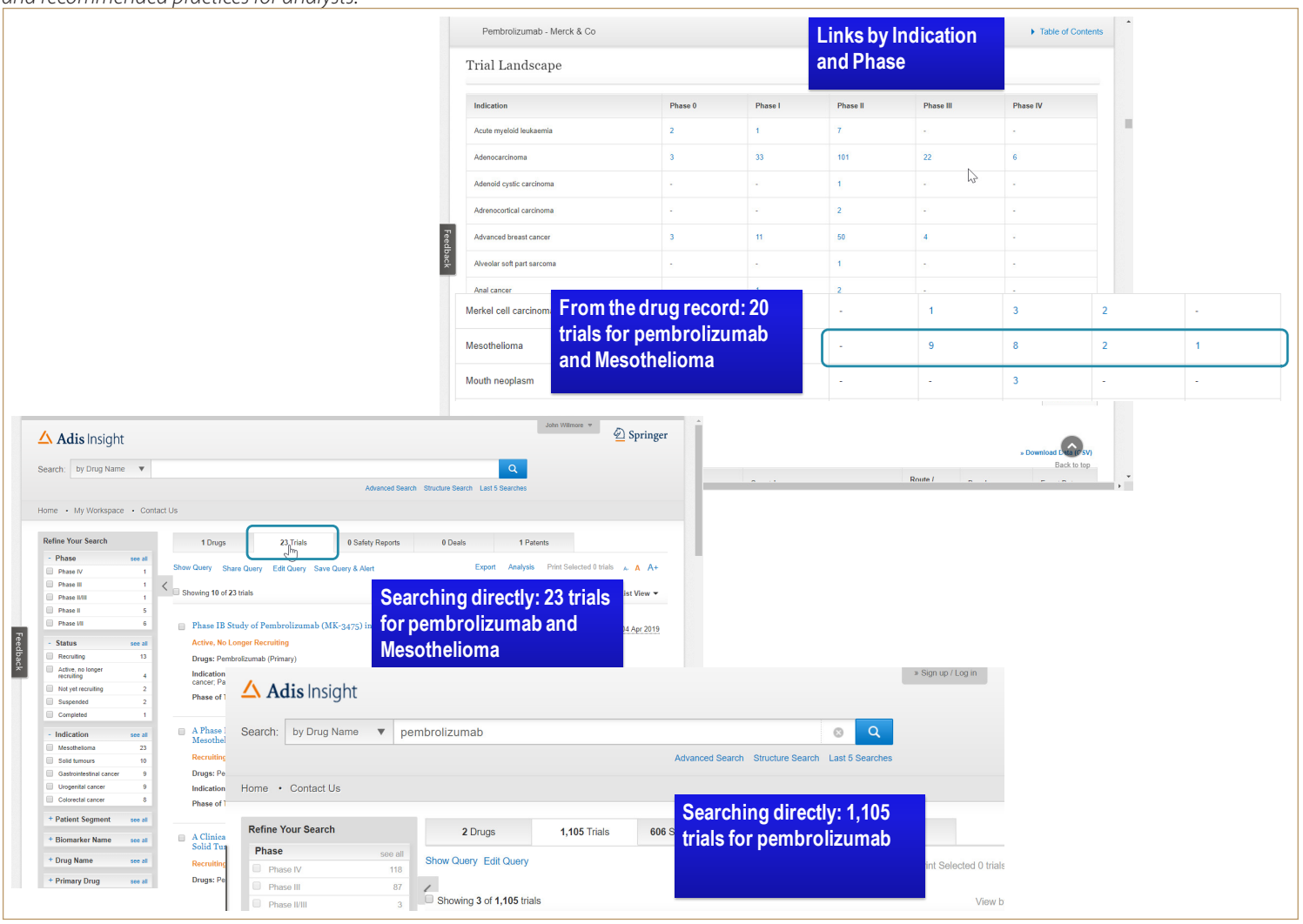
Thoughts from BizInt

Publishers review clinical trial information to decide whether to include an indication in a drug record. Two key considerations are referenced by the panelists: trial phase, and commercial involvement. Adis states their editorial policy to only index the broader indication, such as solid tumors, for early stage trials (Phase I or Phase I/II). Clarivate notes that if a company is not involved with a trial, then that trial will not be considered evidence that the drug is in clinical stage for that indication. But once again, this is an example of an editorial decision. In the case of DS-1647, both Clarivate and Citeline identified a University sponsor for the clinical trial, but one indexed the drug for mesothelioma and one did not. The reason was the determination that the university was in fact acting as the developer of the drug rather than conducting merely academic research. (See footnote below for more Cortellis indexing details.)

1 DS-1647: mesothelioma information in Cortellis is linked to a UMIN trial — UMIN000034063 — from the Tokyo University acting as developer of this drug
Dovitinib: mesothelioma information in Cortellis is present but as discontinued because lack of activity/efficacy
Rebastinib: (mesothelioma information in Cortellis is present from a Deciphera Pharmaceuticals PR with information about a phase 1b/2 trial
BAY-2287411 (mesothelioma information in Cortellis is linked to a Bayer trial — NCT03507452

Example 5(a): Linking drugs and clinical trials — Adis Insight

In this example, we study retrieving clinical trials from a drug record versus searching the clinical trials database directly. Please discuss how drugs and trials are linked between the R&D Insight (drugs) and Adis Clinical Trials Insight (trials) databases, and recommended practices for analysts.



Response from **Adis** *editorial team*

Drug profiles contain links to trials via the trial landscape table and through links to individual trials referenced in the KDM and science sections.

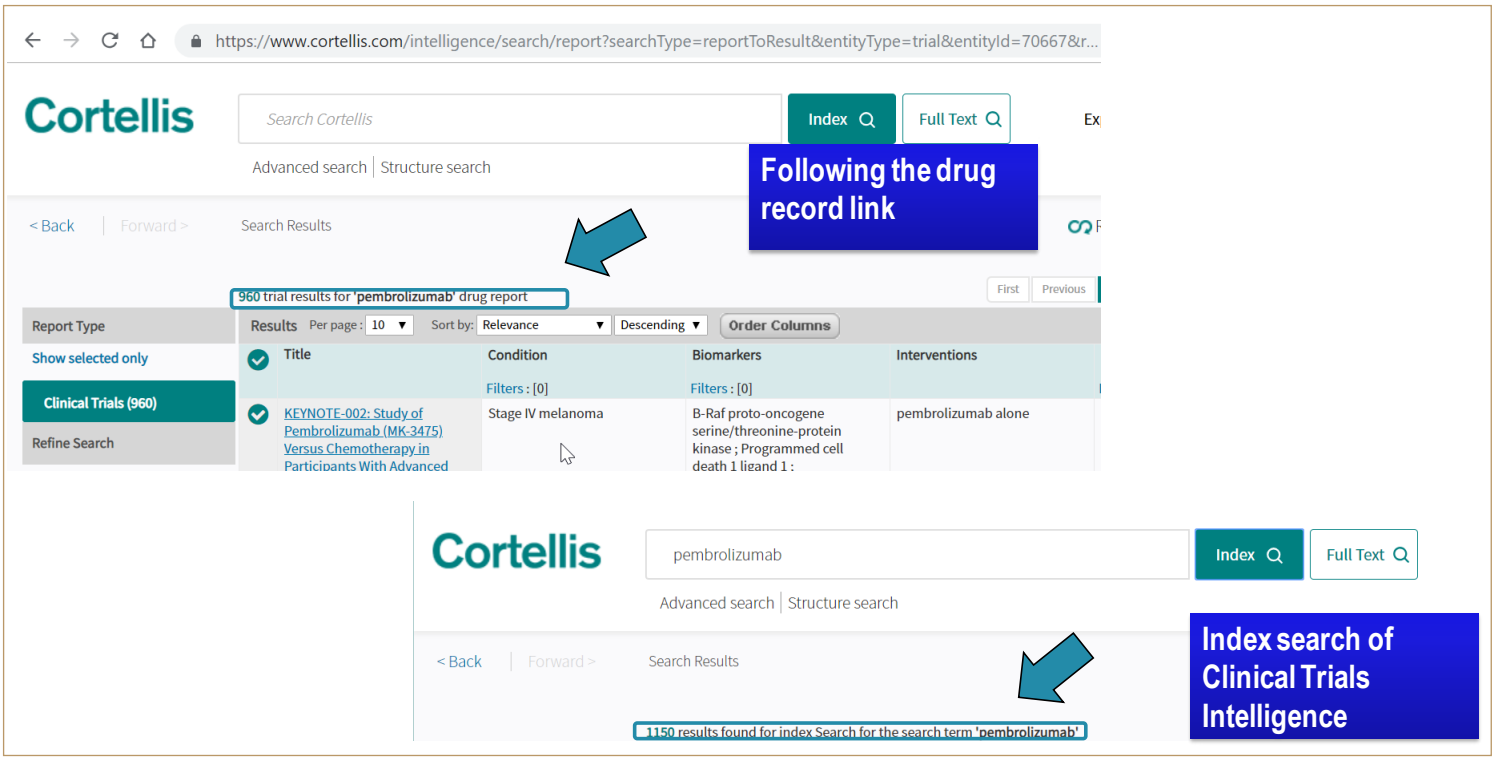
The trial landscape table in the drug profile pulls in all trials that are hard linked to that drug where the drug is the primary drug of focus in the trials. The trials are displayed as numerical links by phase and indication in the table.
The reason why there is a difference in trial numbers between a search for pembrolizumab + mesothelioma (n=23) and the trial number displayed in the pembrolizumab landscape table for mesothelioma (n=20) is because the table contains only the trials where the drug has been used as the primary drug of focus. The other 3 trials in the 'broader' search are trials where pembrolizumab is used in the study but is not the drug of primary focus. Adis Clinical Trials Insight has all trials of any drug that is profiled in Adis R&D Insight, irrespective of whether the drug has been used as the primary drug.

The trials in the trial landscape table can be accessed by clicking through to the set the analyst is interested in. Once they are in the trials module the analyst can use the trials filters to select the studies they are most interested in. Alternatively, they can access the entire trials set from the trials tab in the results (n=23) and then filter the trials by primary drug or whatever else the analyst is interested in investigating.

Drug profiles can be accessed from a trial profile via the link to the primary drug in the At-A-Glance section, or via the 'related drugs' table which contains the other drugs participating in the trial.

Example 5(b): Linking drugs and clinical trials — Cortellis

In this example, we study retrieving clinical trials from a drug record versus searching the clinical trials database directly.
Please discuss how drugs and trials are linked between the Cortellis pipeline and trials databases, and recommended practices for analysts.

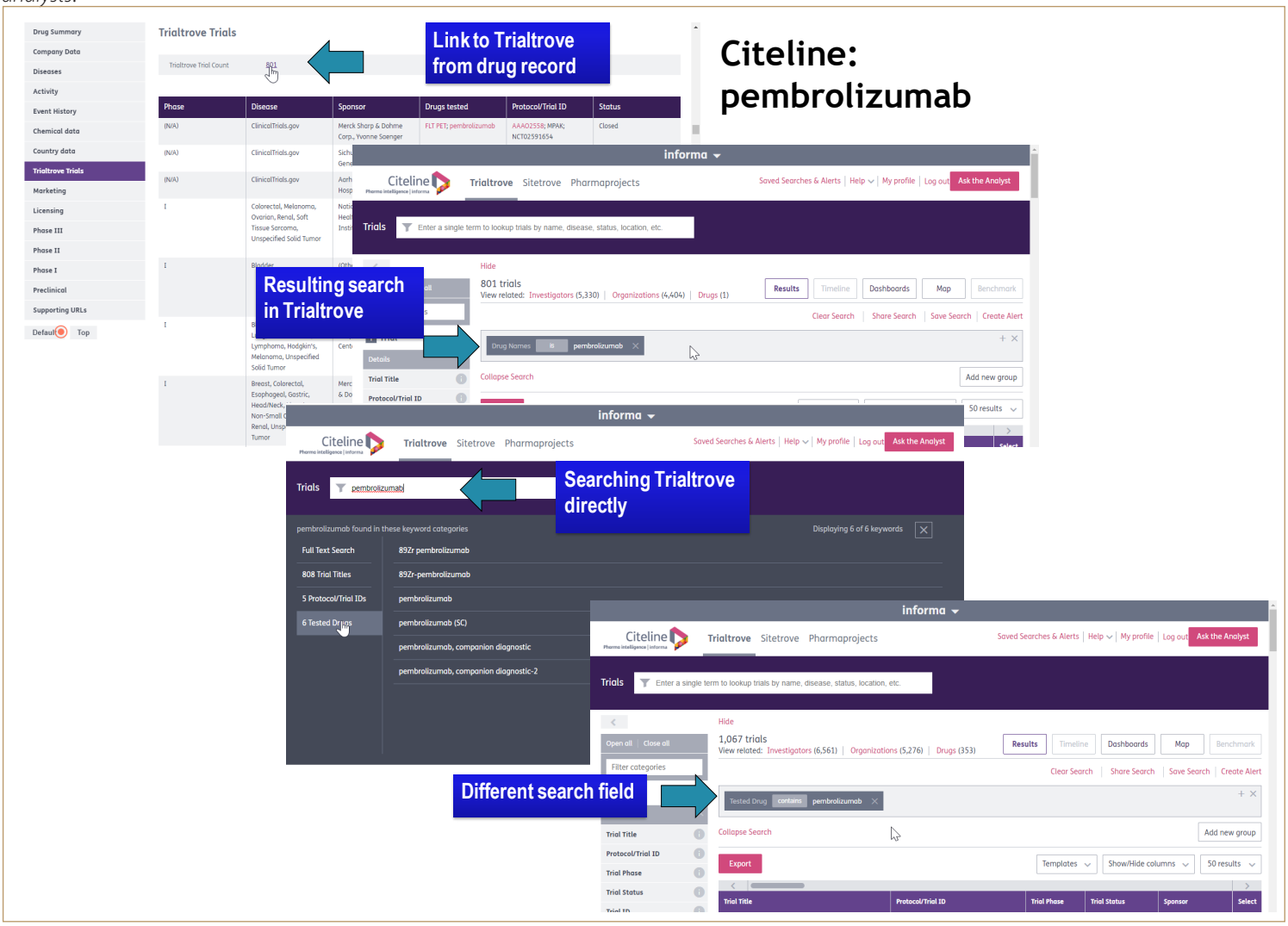


Response from **Cortellis** *editorial team*

The difference in trial count between both the products is due to drug indexing. Results of trials appearing through the drug record consists of trials which are indexed to the drug record; however, the search in the trials database includes trials wherein 'pembrolizumab' is mentioned in any of the free-text fields of non-pembrolizumab trials (eg: patients on pembrolizumab mentioned in the exclusion criteria). Also, the search was conducted in the limited subscription of CTI wherein users can access only trials conducted within USA with no access to results, or additional indexing available on CTI Global. A search in CTI Global would return additional trials.

Example 5(c): Linking drugs and clinical trials — Citeline

In this example, we study retrieving clinical trials from a drug record versus searching the clinical trials database directly.
Please discuss how drugs and trials are linked between the Pharmaprojects (drugs) and Trialtrove (trials) databases, and recommended practices for analysts.



Response from **Citeline** *editorial team*

The link from the pembrolizumab record delivered a list of 801 trials in Trialtrove, all of which include pembrolizumab as a primary drug.

The search starting in Trialtrove was Tested Drug 'contains' pembrolizumab. This resulted in a higher volume of trials because the search also picked up trials where pembrolizumab was an 'other' drug (eg, not the primary drug — possibly where it was a comparator, or an 'add on' drug to a multi-drug regimen). In order to get the results of the two searches to align, the user can further filter the Trialtrove results to show only trials where pembrolizumab is the Primary Tested Drug. By doing so, the resulting cohort of trials will agree with the results delivered by the search that originated in Pharmaprojects.

Thoughts from BizInt

Links from a drug record to matching trials in the publisher's clinical trials database result in a different set of trials from those found when attempting to conduct a simple search for that same drug name. For both Adis and Pharmaprojects, the reason is that the link from the drug record is a search for trials where the drug is the primary drug in the trial. Similarly the link from the drug record in Cortellis is to a set of trials "indexed to the drug record", search whereas the simple search conducted in Cortellis directly appeared to be a free text search, despite being reported on the site as an "index search for the term 'pembrolizumab'."

Conclusions from the Town Hall

A record in a pipeline database represents an editorial view of a drug. Unlike a citation in a literature database, which is based on a single publication, each pipeline record is generally drawn from a broad range of sources.

We deliberately chose three aspects of a drug that might appear at first glance to be reasonably "black and white" — phase, company, and indication. Either a drug is in phase I or it is not. A company either is a licensee developing a drug to treat mesothelioma, or they are not. Though we review only a few examples here, it is clear that the reality is not so simple.

In the editorial responses to the examples, we see many cases where the difference between sources represents a different view of the same information, rather than missed information.

If a drug is in active development, determining when a drug is in a particular phase requires research, but also review and editorial decisions. If a company is acquired after licensing, does the name of the licensee change? What if the acquired company develops the drug largely independent of the parent company?

Searching multiple pipeline databases means you, the analyst, also have editorial decisions to make when preparing an intelligence report. To facilitate this analysis, BizInt Smart Charts software includes the Reference Rows tool to assist in selecting which content to include in integrated reports, with built-in rules and citations to indicate the source for each cell selected for inclusion in the final report.

For More Information

Citeline Pharmaprojects:

The industry's most trusted drug development database, Citeline's Pharmaprojects has been covering pharma R&D across global markets for 35+ years. It's the go-to resource for preclinical, clinical, and pipeline coverage, and lifecycle management tracking.
https://pharmaintelligence.informa.com/products-and-services/data-and-analysis/pharmaprojects

AdisInsight

A database for drug research and development, disease treatment and decision making, based on trusted, scientifically sound data. A single search delivers results on drugs, trials, deals, safety and patents.
https://www.springer.com/gp/adis/products-services/adisinsight-databases

Cortellis Competitive Intelligence

Cortellis Competitive Intelligence™ provides access to data such as drug pipeline, deals, patents, global conferences and company content, along with the latest industry news and press releases.
https://clarivate.com/cortellis/solutions/competitive-intelligence-and-analytics/

BizInt Smart Charts Drug Development Suite

BizInt Smart Charts Drug Development Suite helps you create, customize and distribute tabular reports integrating data from the leading drug pipeline, clinical trials, and biomedical literature databases.
http://www.bizint.com/product/drugdevsuite/

"Surfing the Pipeline" case studies

For previous studies of differences in coverage and content between the different pipeline databases, go to:
http://www.bizint.com/slides#surfing