

Determining lines of therapy (LOT) in oncology in claims databases



Lines of therapy (LOT) and the number of prior lines of therapy influence the clinical benefit and even the magnitude of response to select regimens.¹ They are an important parameter to be determined in retrospective database studies evaluating oncology patients on various chemotherapy/immunotherapy regimens. It is also important to establish LOT regimens for economic outcomes, as resource utilization and costs can then be linked to specific regimens of interest for payers, providers, and patients, helping them to make informed decisions. Since lines of therapy are not explicitly available in claims data, algorithms with rules for initiation, discontinuation, restarting and switching of therapies need to be implemented. This white paper attempts to establish guidelines for determining LOT regimens and durations for retrospective claims studies in oncology.

Start of first line of therapy

The start of the first LOT is usually set as an index date, and is commonly the first date of administration and/or fill of an NCCN-recommended agent for the cancer of interest. Most often, a washout period is set prior to the first infusion to meet the assumption of first line of therapy. Washout periods typically range from three to twelve months, but may be longer in some situations. All chemotherapy/immunotherapy agents filled or administered within a set number of days of the first administration will constitute the first LOT regimen. The number of days used



Establish LOT regimens for economic outcomes.

Resource utilization and costs can be linked to specific regimens of interest for

- payer
- provider
- patient

to determine the regimen for the first LOT typically ranges from three to 30 days, but can be longer (for example, 45/60/90 days) or shorter (for example, only medications on the same day), depending on the study. In oncology, the regimen list for the first LOT can be a single agent or combination of several drugs. The first LOT may represent a planned sequence of various treatments, such as induction therapy, consolidation therapy, stem cell transplantation and maintenance therapy.

End of first line of therapy

Specific criteria exist to determine the end of the first LOT. The earliest occurrence of the following will be used to determine the end of the LOT.

1. Receipt of a chemotherapy/immunotherapy agent not included in the regimen of the first LOT. The end of the LOT is considered the last day before initiating the new agent.
2. Discontinuation of all agents in the first LOT. Discontinuation is defined as a specified gap in therapy (range of 30–180 days, usually) following the run-out date. For medications received through the pharmacy, the run-out date is defined as: fill date + days' supply minus 1. For physician-administered medications, a presumed days' supply of 14–30 days is used. The length of the presumed days' supply depends on the expected cycle length. In this situation, the end of the LOT will be considered the latest run-out date leading to discontinuation. For most cancer regimens, if only a single agent or portion of the total regimen is discontinued of a multi-drug regimen, this is not considered a new LOT.
3. End of study period.
4. Disenrollment from health plan.
5. Death.

In some cancers, interventions other than chemotherapy/immunotherapy initiations are also considered to end a LOT. Examples of such interventions include stem cell transplant (SCT) for hematological cancers, or radiation treatment for certain solid cancers.

If the end of the study period or disenrollment is identified as the reason for the end of the LOT, that LOT is considered censored rather than completed. The identification of a LOT as either completed or censored impacts the clinical and economic outcomes of interest. These can be compared and calculated, and are an important consideration when reporting study results.

Subsequent lines of therapy

Many reasons exist for change in treatments. These reasons may include end of planned regimen, toxicities, progression, inadequate response, patient preference and insurance benefit changes. Claims database studies do not capture the reason for a change. Receipt of a chemotherapy/immunotherapy agent after the end of the first LOT initiates a second LOT; and the start and end of subsequent LOTs are identified using the logic described above.

Stem cell transplants indicate a change in therapy. They may end a previous LOT or start a new LOT, depending on the cancer. If the SCT is planned as part of the induction and consolidation, then it is part of the previous line; otherwise, SCT is a new LOT.



The identification of a LOT impacts the clinical and economic outcomes of interest.

Maintenance lines of therapy

Maintenance LOTs are considered part of the active LOT that they follow. Rules surrounding maintenance LOTs may include some of the following considerations:

- The LOT contains an individual drug or combination of drugs from the regimen of the active LOT immediately prior, that is, the regimen is a subset of the prior regimen.
- The LOT contains specific monotherapy drugs as recommended by NCCN guidelines for maintenance.
- The LOT starts within a certain number of days after the end of the active LOT.
- The duration of the LOT is a certain period of length.

Interruptions and dose modifications

Regimens that are interrupted can be considered restarts of the same LOT or incremented to the next LOT depending on the length of the interruption. Usually, if the interruption is less than the gap identified as a true discontinuation, then restart of the same line does not increment the LOT. However, if the interruption is longer than the time set for a true discontinuation, then the LOT is incremented. Likewise, if another agent or a combination of agents is given in between the restart of the previous LOT, then the LOT is incremented. In cancers such as multiple myeloma, where rechallenge in relapse setting is quite common, the period of the interruption determines if the LOT is incremented or not. Dose modifications are not considered as increments to the LOT.

We believe that establishing rules and guidelines to determine LOT in claims-based retrospective studies in oncology is essential to determining the clinical benefit and the economic impact of specific treatment regimens. We hope this paper provides a framework to initiate the process in your study setting to answer your specific research questions.

To learn more about our data assets and expertise and how they can strengthen your work, please contact us.

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1. Rajakumar SV, Richardson P, San Miguel JF. Guidelines for determination of the number of prior lines of therapy in multiple myeloma. *Blood*. 2015 Aug 13;126(7):921-2.



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