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Use of epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors for the treatment of lung cancer in the Québec context

English summary

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SUMMARY

Use of epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors for the treatment of lung cancer in the Québec context

INESSS has undertaken a major three-part project to explore the potential of clinical administrative data as a lever for improving cancer care practices [INESSS, 2021]. The present work concerns the part dealing with the assessment of the value of innovative therapies in the Québec real-world context. The primary objective was to estimate overall survival in patients receiving an epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI; gefitinib, afatinib or osimertinib) for the treatment of lung cancer in three indications and to determine whether these results are similar to those reported in published studies. The project's objectives also included providing a picture of the use of EGFR-TKIs in Québec, assessing these results in relation to the clinical practice recommendations and published data, and proposing certain avenues for improving practices. Lastly, the work sought to better understand the possibilities, limitations and issues related to this type of assessment in the real-world care context.

For this purpose, a global cohort of patients who received an EGFR-TKI between April 1, 2001 and March 31, 2019 was first created. Then, three cohorts corresponding to the indications of interest were created, specifically, with the use of a classification algorithm according to the line of treatment of the first EGFR-TKI received.

The work carried out shows that it is possible to provide a picture of the use of certain innovative therapies and to estimate their value in the Québec real-world context using clinical administrative databases (CADBs). However, this exploration also shows that certain useful data are not available, which poses limitations regarding the types of therapies and the indications that can be evaluated and the evaluation methods that can be used. Only drugs dispensed in community pharmacies and covered by Québec's public prescription drug insurance plan can be evaluated with the CADBs. In addition, the drugs that lend themselves best to this type of evaluation are those whose indications are confined to a limited number of clinical situations and whose coverage is well defined.

Furthermore, it appears that it may take a relatively long time to obtain reasonably accurate results concerning median overall survival.

The findings from the present work are listed below. They concern only patients whose EGFR-TKIs were covered by Québec's public prescription drug insurance plan.

General overview of EGFR-TKI[1] use in Québec between April 1, 2001 and March 31, 2019

- As at March 31, 2019, 679 patients had received at least one EGFR-TKI.
- In 2018-2019, the most recent fiscal year with complete data:
  - 4375 EGFR gene mutation tests were performed in Québec laboratories;
  - 199 physicians prescribed at least one EGFR-TKI;
  - 217 patients started therapy with an EGFR-TKI.

Use of EGFR-TKIs in Québec for the three indications of interest

Patient numbers and characteristics

- As at the patient inclusion (March 31, 2019) and follow-up (EGFR-TKI use and survival; March 31, 2020) cut-off dates:
  - 457 had started therapy with gefitinib as first-line palliative treatment;
  - 80 had started therapy with afatinib with the same intent;
  - 119 had started therapy with osimertinib, after another EGFR-TKI given as first-line palliative therapy.
- A higher proportion of women than men received gefitinib (68.5%), afatinib (60.0%) or osimertinib (70.6%), which is consistent with published data on the frequency of EGFR mutations in men and women.
- Patients aged 80 years and older had access to EGFR-TKIs. They accounted for 7.5% to 20.2% of the patients who received an EGFR-TKI, depending on the indication. Patients up to 93 years of age started therapy with an EGFR-TKI. While toxicity may be a barrier to the use of chemotherapy in patients this old, there is evidence to support the use of EGFR-TKIs in these patients.
- Depending on the indication, 70% to 77% of the patients had between 0 and 9 comorbidities, and about 7% to 10% had 15 or more comorbidities.

Treatments received before the first EGFR-TKI

- An EGFR-TKI was the first treatment administered after a lung cancer diagnosis in 40.7% of the patients who received first-line gefitinib and in 31.3% of those who received first-line afatinib.
- 22.3% of the patients who received first-line gefitinib and 12.5% of those who received first-line afatinib had previously been treated with lung resection surgery. In the selected studies, this proportion ranged from 10% to 41%.
- Gefitinib was the first-line therapy for more than three-quarters (77%) of the patients who received osimertinib after another EGFR-TKI as first-line therapy.

[1] Include gefitinib, afatinib and osimertinib, and exclude erlotinib and dacomitinib.

Number of days of EGFR-TKI dispensed

- The median number of days of EGFR-TKI dispensed in community pharmacies per patient ranged from 274.5 to 300 days (9.0 to 9.9 months), depending on the indication. The longest number of days of EGFR-TKI dispensed (maximum) was observed with gefitinib (2400 days, or 6.6 years).
- As an indication, the median number of days for which gefitinib or osimertinib was dispensed was very similar to the medians for progression-free survival reported in the pivotal studies, but the difference between these two endpoints was somewhat greater for afatinib. Although the number of days of medication dispensed may, in some situations, be similar to that for progression-free survival, these endpoints are not equivalent.

Overall survival in patients who received an EGFR-TKI and comparison with published study results

- Median overall survival for those who received gefitinib as first-line palliative therapy was 18.9 months (95% CI: 16.3 - 21.9). Taking the margins of error into account, this result suggests that the overall survival achieved in Québec:
  - Was not different from that in IPASS, one of the two studies submitted to INESSS for an evaluation for coverage purposes;
  - Was not different from that in most of the studies selected for the comparison.
- Median overall survival in the patients who received afatinib as first-line palliative therapy was 26.6 months (95% CI: 13.7 - not evaluable). However, the data are still immature, and this value could change significantly with a longer follow-up. According to the current estimate, this result suggests that overall survival in Québec:
  - Is not different from that in LUX-Lung 3 or LUX-Lung 6, the two studies submitted to INESSS for an evaluation for coverage purposes;
  - Is not different from that in all the randomized controlled trials (RCTs) and most of the published real-world studies (RWSs).
- Median overall survival in the patients who received osimertinib after another EGFR-TKI as first-line palliative therapy was 19.9 months (95% CI: 17.4 - not evaluable). However, the data are still immature, and this value could change significantly with a longer follow-up. According to the current estimate, this result suggests that overall survival in Québec:
  - Is lower than that in AURA3, the study submitted to INESSS for an evaluation for coverage purposes;
  - Is not different from most of the results of the studies that have evaluated this drug in a real-world setting.

Assessment of the state of Québec practice and avenues of improvement

- The expected number of patients who would need to receive an EGFR-TKI annually is not known, and it cannot be estimated with the available data.
- In the Québec context, EGFR-TKIs appear to provide expected results or at least results similar to those obtained in real-world settings in other parts of the world. Thus, it is important to reiterate that EGFR-TKIs should be offered to all eligible patients in line with the recognized indications (see Section 2.1 and *Algorithmes d'investigation, de traitement et de suivi*).
- For a small proportion of the patients, EGFR-TKIs were prescribed in a line or sequence of treatment not recognized in Québec and not recommended in the *Algorithmes d'investigation, de traitement et de suivi*. In particular, gefitinib or afatinib was prescribed to some patients as second-line treatment after palliative chemotherapy, and they were used as successive lines of treatment in others.
- The analyses suggest that it took about 5 years before EGFR-TKIs were fully integrated into Québec practice. However, some clinicians seem to have been particularly proactive in integrating osimertinib into their practice. A few avenues should be considered to speed up access to novel therapies, especially when the eligibility criteria are based on new paradigms:
    - Provide service corridors to facilitate access to companion tests in all regions of Québec and resources for providing the results in a timely manner;
    - Improve the dissemination of information on the availability of novel therapies to administrators and clinicians;
    - Promote the dissemination of this information to patients and patient associations.

Elements to be taken into consideration regarding the evaluation of therapies in the Québec real-world context

- Two main elements should be taken into consideration regarding the feasibility of evaluating a therapy in the Québec real-world context:
    - The availability of the data required for the evaluation.

      These data should enable one to:
        - Sensitively and specifically identify those who have received the therapy and those who have received the comparator treatment, if applicable;
        - Calculate the decisional endpoint;
        - Choose a valid design and criteria for drawing conclusions.

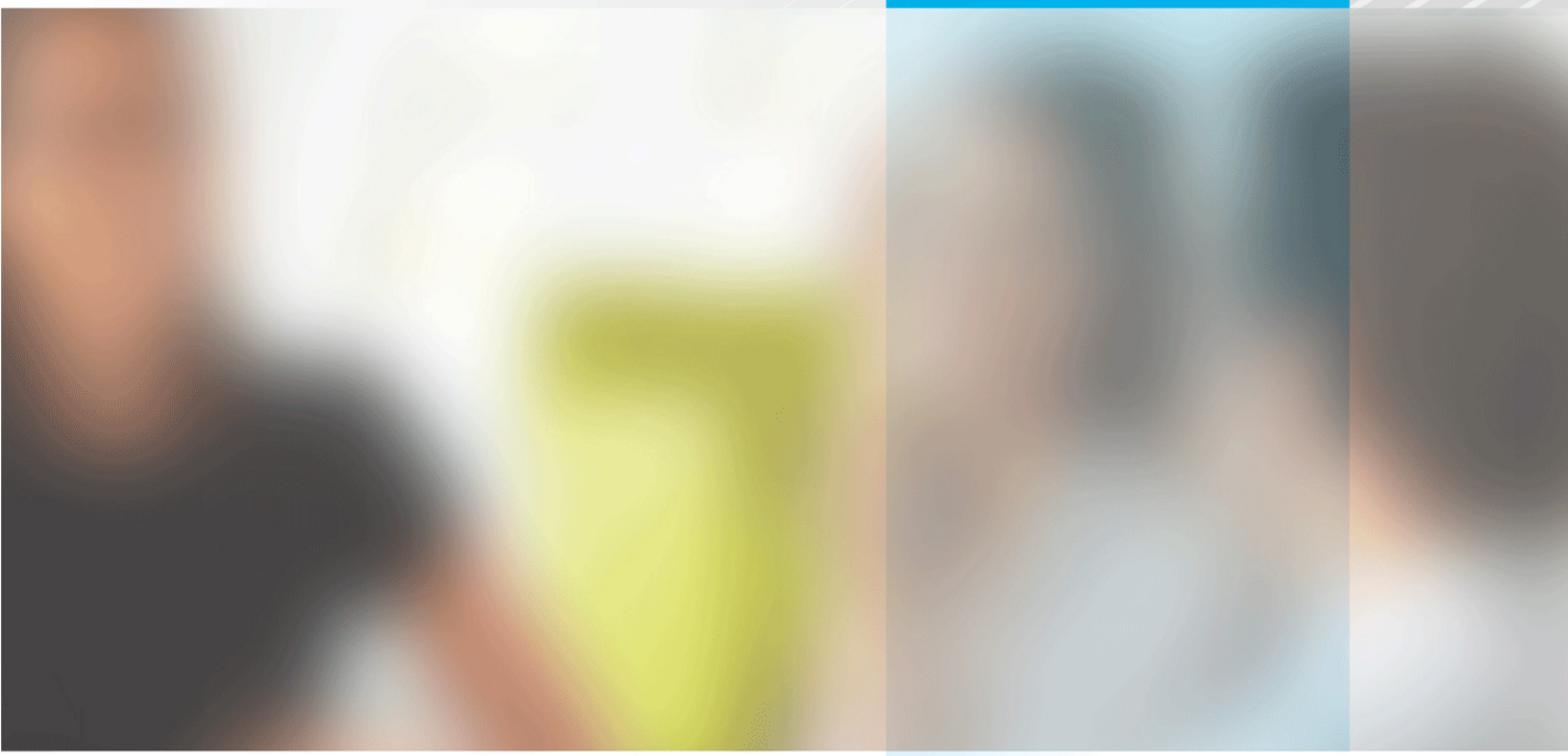
- Having a realistic timeframe for obtaining results with acceptable accuracy according to the purpose of the evaluation.

  This timeframe will depend mainly on:

  - The number of patients who receive the therapy and for whom data are available;
  - The time to the occurrence of the endpoint event;
  - The effect size of the experimental therapy relative to the comparator treatment, if applicable.

Outlook

The third part of this exploratory project is underway. Its objectives are to characterize the clinical trajectories of lung cancer patients in the Québec real-world context, to assess these trajectories relative to the clinical practice guidelines, and to identify any heterogeneous practices. In time, the most useful results of the three parts of this project can be updated on a regular basis, other questions aimed at improving care can be addressed, and the methods developed for the study of lung cancer can possibly be adapted for other types of cancer.



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