Osimertinib First-Line Approval in Epidermal Growth Factor Receptor (EGFR) Mutation-Positive Metastatic Non-Small Cell Lung Cancer (NSCLC) Impact on Utilization and Total Cost of Care among 15 Million Commercially Insured Members

J.J. Whalen, PharmD, BCOP[1,2]; D.J. Eckwright, PharmD[1]; J.P. Burke, PhD, MPH[1]; P.P. Gleason, PharmD[1,2]. [1]Prime Therapeutics LLC, Eagan, MN, United States; [2]University of Minnesota College of Pharmacy, Minneapolis, MN, United States.

No external funding provided for this research

BACKGROUND

- Lung cancer is the 2nd most common form of cancer for men and women and is the leading cause of cancer death in the U.S.[1]
- Most lung cancer cases (84%) are non-small cell lung cancer (NSCLC), with 10% to 50% having an Epidermal Growth Factor Receptor (EGFR) mutation.[2,3]
- Metastatic NSCLC patients with an EGFR mutation are treated with chronic oral EGFR inhibitor (EGFR-i) therapy — afatinib (Gilotrif®), dacomitinib (Vizimpro®), erlotinib (Tarceva®), gefitinib (Iressa®), or osimertinib (Tagrisso®) — until progression or unacceptable toxicity.[3]
- Osimertinib was FDA-approved[4] for second-line use in November 2015 with second-line pricing, an annual wholesale acquisition cost (WAC) of $177,152, which is 1.7-fold higher than the initial first-line EGFR-is (afatinib, erlotinib, gefitinib).
- In Sept 2017, National Comprehensive Cancer Network (NCCN) changed their guidelines to include osimertinib as a preferred first-line therapy for NSCLC, and in April 2018, osimertinib gained FDA approval for first-line use.[5,6]
- Although osimertinib gained a first-line indication, it maintained its second-line pricing making it important for payers and stakeholders to understand its first-line utilization trend and impact on total cost of care (TCC), as well as value-based contracting and management opportunities.

OBJECTIVE

Using 15 million commercially insured members integrated medical and pharmacy claims, determine the real-world:

- Osimertinib utilization trend for members new to EGFR-i therapy.
- Average member TCC 6-months pre- and post-initiation of EGFR-i therapy; comparing osimertinib TCC to competitor EGFR-is (cEGFR-is).
- Discontinuation rate among members newly initiating EGFR-i therapy; comparing osimertinib to cEGFR-is.

4085-G © Prime Therapeutics LLC 10/19
2900 Ames Crossing Road, Eagan, MN 55121
AMCP, October 2019, National Harbor, MD, USA
PATRICK GLEASON, 800.858.0723, ext. 5190
pgleason@primetherapeutics.com

METHODS

All analyses were conducted using integrated medical and pharmacy administrative claims data from 15 million commercially insured members.

Proportion of Members Newly Initiating EGFR-i Therapy using Osimertinib

- EGFR-is with NSCLC FDA-approved indication, afatinib, dacomitinib, erlotinib, gefitinib, and osimertinib, were included in this study.
- Pharmacy claims were queried from January 2017 to June 2019 for EGFR-i claims using Generic Product Identifier (GPI) codes for osimertinib (215340652003xx) and cEGFR-is (215340061003xx, 21534025 1003xx, 215340190003xx and 215340300003 20).
- A member's first EGFR-i claim found during January 2017 to June 2019 was defined as their index date and index drug.
- Members were required to be continuously enrolled six months before (pre-period) their index date.
- Members were required to be newly initiating EGFR-i therapy defined as no EGFR-i claims in the pre-period.
- EGFR-i utilizers were trended quarterly by proportion of osimertinib compared to cEGFR-is from January 2017 to June 2019. Note: No dacomitinib claims were found.

Analytic Population Identification for EGFR-i Discontinuation Assessment and TCC Assessment

- New start EGFR-i members during January 2017 to December 2018 (2 years) were identified and those continuously enrolled six months before (pre-index) and six months after (post-index) their initial EGFR-i claim were included for the discontinuation and TCC analyses.
- NSCLC Diagnosis: All members meeting continuous enrollment criteria newly initiating EGFR-i therapy with osimertinib or a cEGFR-i had their medical claims evaluated for presence of at least one claim with lung cancer diagnosis, ICD-10 code beginning with C34.xx in any of five positions on a medical claim during the continuous enrollment pre/post periods. Prevalence of lung cancer diagnosis by new start members by drug is reported.

Discontinuation Among New Start Members, Osimertinib vs Competitor EGFR-is

- Members identified as new to EGFR-i therapy in the previous analysis were used to evaluate discontinuation.
- Discontinuation was defined as a 30-day or greater gap in therapy after the end of their initial EGFR-i claim plus days supply among new starts. For example, an afatinib claim occurred on Jan. 1, 2018 with a 30-day supply. Discontinuation would be declared if the member had no subsequent afatinib claims by March 1, 2018 ([Jan. 1, 2017 + 30-day supply) − 1 + 30-day gap).
- Days on therapy prior to discontinuation (30-day gap) was then evaluated by 30-day intervals for osimertinib and cEGFR-is to understand timing of discontinuation. cEGFR-i utilizers were only counted as discontinued if they discontinued all agents within the group. Therefore, switching between groups, e.g., the cEGFR-i to osimertinib would not extend members days on therapy and constitutes discontinuation.
- The difference in discontinuation rates between osimertinib and competitive EGFR-i groups was compared with a chi-squared test.

Average 6-Month Pre- and Post-Total Cost of Care (TCC) among Members Newly Initiating EGFR-i Therapy, Osimertinib vs Competitor EGFR-is

- Pharmacy and medical claim allowed costs, after network discounts, were analyzed in this study. Costs included member and plan paid allowed. At the member level, the sum of all health care claims costs was defined as TCC during the analysis period, i.e., EGFR-i index date pre- or post- period were summed and averaged for members newly initiating EGFR-i by osimertinib group and the cEGFR-i therapies group. TCC was broken into the following:
  - All medical benefit costs.
  - All pharmacy benefit costs, excluding EGFR-i costs.
  - EGFR-i costs.
- EGFR-i TCC sub-analyses were performed limited to members with a NSCLC diagnosis and limited to members who remained EGFR-i persistent, i.e., did not discontinue EGFR-i, during the post-period.

RESULTS

Proportion of Members Newly Initiating EGFR-i Therapy using Osimertinib (Figures 1 and 2)

- Among 15 million commercially insured members, during January 2017 through June 2019, 1,020 members with a claim for an EGFR-i were identified. 768 (75.3%) of 1,020 members were continuously enrolled six months prior to their first EGFR-i claim and 492 (48.2%) were identified as new starts to EGFR-i therapy.
  - During the 2.5 years assessed, per quarter an average of 49 members (range 37 to 61) were new to EGFR-i therapy.
  - Osimertinib new starts among all EGFR-is new starts accounted for 6.9% (4 of 58) in the first quarter of 2017 as compared to 71.1% (32 of 45) in the second quarter of 2019, a ten-fold increase.

Average 6-Month Pre- and Post-TCC Among Members Newly Initiating EGFR-i Therapy, Osimertinib vs Competitor EGFR-is (Figure 1, Figure 3)

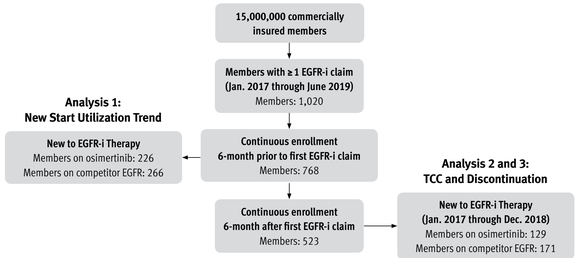
- From January 2017 to December 2018, 523 members with an EGFR-i claim were continuously enrolled in the pre- and post-period and 300 (57.4%) members were new starts.
  - 129 (43.0%) and 171 (57.0%) initiated osimertinib and cEGFR-is, respectively.
  - 261 (87.0%) of 300 new start members with a lung cancer diagnosis meeting continuous enrollment criteria:
    - Osimertinib — 117 (90.1%) of 129 members.
    - cEGFR-is — 144 (84.2%) of 171 members:
      - Afatinib: 68 (93.2%) of 73 members.
      - Erlotinib: 69 (75.8%) of 91 members.
      - Gefitinib: 7 (100.0%) of 7 members.
- cEGFR-i 171 users mean TCC pre-period was $71,520 and $85,745 post-period, a 19.9% increase.
  - A subset of 144 cEGFR-i users with NSCLC had a TCC of $76,367 pre-period and $89,632 post-period, a 17.4% increase.
  - A subset of 104 cEGFR-i persistent users had a TCC of $63,481 pre-period and $83,877 post-period, a 32.1% increase.
  - A subset of 90 cEGFR-i persistent users with NSCLC had a TCC of $68,893 pre-period and $86,826 post-period, a 26.0% increase.
- Osimertinib — 129 users mean TCC pre-period was $58,221 and $123,679 post-period, a 112.4% increase.
  - A subset of 117 osimertinib users with NSCLC had a TCC of $62,283 pre-period and $126,966 post-period, a 103.9% increase.
  - A subset of 102 osimertinib persistent users had a TCC of $60,589 pre-period and $128,931 post-period, a 112.8% increase.
  - A subset of 94 osimertinib persistent users with NSCLC had a TCC of $65,697 pre-period and $131,355 post-period, a 99.9% increase.
- Non-EGFR-i pharmacy costs account for 3% of total costs for both cEGFR-i and osimertinib groups, compared to 7.5% and 2.6% of total costs in the post-period for cEGFR-i and osimertinib groups, respectively.
- Post-period EGFR-i only costs averaged $42,286 for the cEGFR-i group and $88,706 for the osimertinib group, for a 109.8% higher average cost in the osimertinib. Among the subsets, osimertinib costs were:
  - 105.5% higher in NSCLC only comparison.
  - 90.8% higher in persistent only comparison.
  - 94.6% higher in persistent and NSCLC comparison.
- Osimertinib group mean post-period TCC was $37,934 higher versus cEGFR-i group, with the EGFR-i therapy cost accounting for 49.3% in the cEGFR-i group and 71.7% in osimertinib group. Among the subsets, the osimertinib group post-period TTC costs were:
  - $37,334 higher in NSCLC only comparison.
  - $45,054 higher in persistent only comparison.
  - $44,529 higher in persistent and NSCLC comparison.

Discontinuation Among New Start Members, Osimertinib vs Competitor EGFR-is (Table 1)

- 18.6% (24 of 129) of osimertinib new starts discontinued therapy in the post-period compared to 33.9% (58 of 171) of cEGFR-i users, p<0.001. Three members switched within cEGFR-i group.
- 4 (3.1%) of 129 of osimertinib new starts switched to another EGFR-i therapy in the post-index period compared to 14 (8.2%) of 171 cEGFR-i users switched to osimertinib, p=0.086.

FIGURE 1

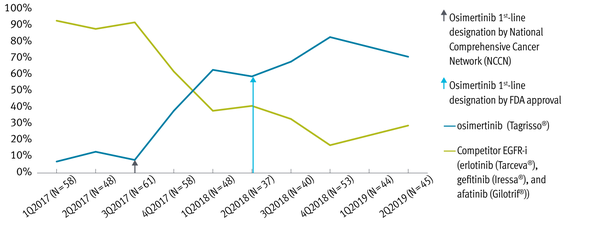
Identification of Members Newly Starting EGFR-i Therapy



EGFR-i = Epidermal Growth Factor Receptor inhibitor. TCC = Total Cost of Care.
Competitor EGFR-is = erlotinib (Tarceva®), gefitinib (Iressa®), and afatinib (Gilotrif®). No dacomitinib (Vizimpro®) claims were identified during time of analysis.
EGFR-i claims were identified using pharmacy claims for approximately 15 million commercially insured members from January 2017 through June 2019. Members new to EGFR-i therapy were defined as having no previous EGFR-i claim in the 6 months prior to their first EGFR-i claim.

FIGURE 2

Proportion of Members New to EGFR-i Therapy: Osimertinib vs Competitor EGFR-is Quarterly among 15 Million Commercially Insured Lives



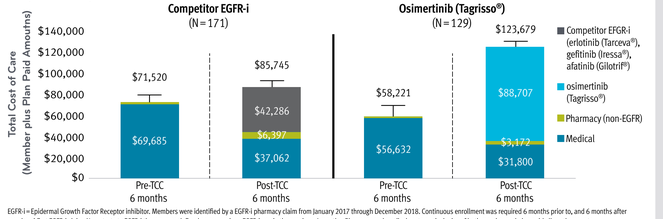
EGFR-i = Epidermal Growth Factor Receptor inhibitor.
Members were identified as having a pharmacy claim for an EGFR-i from January 2017 through June 2019. Members were required to have continuous enrollment 6 months prior to their first EGFR-i claim. Members newly initiating EGFR-i therapy were defined as having no previous EGFR-i claim in the 6-month period prior to their identified EGFR-i claim. No dacomitinib (Vizimpro®) claims were identified during time of analysis.

LIMITATIONS

- Administrative pharmacy and medical claims have the potential to be miscoded and include assumptions of members' actual drug use and diagnoses.
- Members were only confirmed to be new to EGFR-i therapy; other methods of therapy (e.g., surgery, radiation, non-EGFR-i drugs) were not evaluated or controlled for in this study.
- Members were not stratified by severity of illness, performance status, or treatment outcomes: disease progression, progression free survival, or overall survival.
- Several different methods for determining discontinuation exist. This analysis used a 30-day gap to describe discontinuation rates and other methods would generate different results. Our data showed 99% of claims had a 30-day supply or less, which strengthens our use of a 30-day gap.
- Claim costs were not adjusted for site of care (e.g., facility, professional or pharmacy) which can contribute to differing cost markups.
- Two of the cEGFR-is had FDA-approved indications to treat other cancers besides NSCLC. Therefore, osimertinib TCC comparisons may be most appropriately compared limited to the lung cancer diagnosed subset. In addition, osimertinib users had significantly higher persistence. A subset analysis including only persistent members was performed and the substantially higher osimertinib TCC findings remained.
- The data used in this study was limited to a commercial population and results are not generalizable to Medicare or Medicaid populations.

FIGURE 3

Average Total Cost of Care for Members Newly Initiating EGFR-i Therapy 6 Months Pre- and Post-initial EGFR-i Claim: Osimertinib (Tagrisso®) Compared to Competitor EGFR-is



EGFR-i = Epidermal Growth Factor Receptor inhibitor. Members were identified by a EGFR-i pharmacy claim from January 2017 through December 2018. Continuous enrollment was required 6 months prior to, and 6 months after members' first EGFR-i claim. New starts to EGFR-i therapy was defined as no previous EGFR-i use in the previous 6 months. Pharmacy and medical costs are inclusive of both member and plan paid allowed amounts.
No dacomitinib (Vizimpro®) claims were identified during time of analysis. TCC = Total Cost of Care.
Total cost of care 95% interval is indicated by the extended line above the top of each bar.

TABLE 1

Discontinuation for Members Newly Initiating EGFR-i Therapy in the 6-month Post-Period

	Competitor EGFR-i N=171			Osimertinib (Tagrisso®) N=129		
Days on Therapy Prior to Discontinuation	N	%	Cumulative %	N	%	Cumulative %
1 to 30	13	7.6%	7.6%	6	4.7%	4.7%
31 to 60	12	7.0%	14.6%	6	4.7%	9.3%
61 to 90	11	6.4%	21.1%	5	3.9%	13.2%
91 to 120	13	7.6%	28.7%	4	3.1%	16.3%
121 to 152	9	5.3%	33.9%	3	2.3%	18.6%
Total Discontinued Members	**58 of 171**		**33.9%**	**24 of 129**		**18.6%**

EGFR-i = Epidermal Growth Factor Receptor inhibitor.
Competitor EGFR-is = erlotinib (Tarceva®), gefitinib (Iressa®), and afatinib (Gilotrif®). No dacomitinib (Vizimpro®) claims were identified during time of analysis.
Members were identified by a EGFR-i pharmacy claim from January 2017 through December 2018. Continuous enrollment was required 6 months prior to and 6 months after the initial EGFR-i claim. New starts were defined as no previous EGFR-i use in the previous 6 months. Discontinuation was defined as a a 30-day gap in therapy after the end of their initial EGFR-i claim plus days supply.
Using Chi-Squared test, discontinuation was significantly lower with osimertinib vs competitor EGFR-is (p<0.001).

CONCLUSIONS

- In this real-world analysis of 15 million commercially insured members, new start EGFR-i therapy (i.e., afatinib, dacomitinib, erlotinib, gefitinib, or osimertinib) is over 70% osimertinib, a ten-fold increase since osimertinib received a NSCLC first-line NCCN guideline recommendation.
- The dramatic increase in osimertinib first-line EGFR-i use is concerning to payers as the annual wholesale acquisition cost is more than $70,000 higher than competitor EGFR-is. Our real-world total cost of care (TCC) 6-month post initiation findings confirm higher costs versus competitor EGFR-is at $37,934, equating to over $4 million in additional costs for 129 osimertinib treated members.
- Some of the higher osimertinib treated members' TCC could be attributed to the 15-percentage point higher persistence compared to members utilizing competitor EGFR-is. However, when only persistent osimertinib and competitor EGFR-i utilizers were compared, the TCC 6-month difference was $45,054 higher among osimertinib utilizers.
- Osimertinib $177,152 annual wholesale acquisition cost coupled with the finding that 1 in 6 discontinue therapy during the first 6 months warrants the need for value-based contacting to recoup the drug cost waste associated with therapy failure.
- These findings provide foundational understanding of osimertinib discontinuation and total cost of care for value-based contracting and pharmacy management opportunities.

REFERENCES

1. American Cancer Society: Key Statistics for Lung Cancer. Atlanta, Ga: American Cancer Society, 2019. Revised Jan 8, 2019 (https://www.cancer.org/cancer/non-small-cell-lung-cancer/about/key-statistics.html) last accessed on Sept 16, 2019.
2. American Cancer Society: Cancer Facts and Figures 2019. Atlanta, Ga: American Cancer Society, 2019. (https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf) last accessed on August 26, 2019.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines ®) Non-Small Cell Lung Cancer Version 7.2019. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf last accessed Sept 16, 2019.
4. Tagrisso™ (AZD9291) approved by the US FDA for patients with EGFR T790M mutation-positive metastatic non-small cell lung cancer. AstraZeneca Nov, 2015. https://www.astrazeneca.com/media-centre/press-releases/2015/TAGRISSO-AZD9291-approved-by-the-US-FDA-for-patients-with-EGFR-T790M-mutation-positive-metastatic-non-small-cell-lung-cancer-13112015.html#.
5. Tagrisso® (osimertinib) granted Breakthrough Therapy Designation by US FDA for the 1st-line treatment of patients with EFGR-mutation positive non-small cell lung cancer. AstraZeneca Oct, 2017 https://www.astrazeneca-us.com/media/press-releases/2017/tagrisso-osimertinib-granted-breakthrough-therapy-designation-by-us-fda-for-the-1st-line-treatment-of-patients-with-egfr-mutation-positive-non-small-cell-lung-cancer-10092017.html.
6. FDA Drug Approvals and Databases. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-osimertinib-first-line-treatment-metastatic-nsclc-most-common-egfr-mutations last accessed on August 26, 2019.

03010622