CARE™ PERSPECTIVES
ASCO 2020
LUNG CANCER SECTION
AMERICAN SOCIETY OF CLINICAL ONCOLOGY
MAY 29 - 31ST 2020
The American Society of Clinical Oncology (ASCO) recently hosted the virtual annual meeting May 29th-31st, 2020. This CARE™ Update from ASCO focuses on trials presented in lung cancer. Full abstract and session presentation content are available at: https://meetinglibrary.asco.org/browse-meetings/2020%20ASCO%20Virtual%20Scientific%20Program

In this chapter of the CARE™ Perspectives ASCO Conference Report:

01 - Lung Cancer Plenary and Oral Session Highlights
- ADAURA
- CTONG1104
- DESTINY-Lung01
- NEJ026
- Clinical Science Symposium- MET Mutations: The Meat of the Matter

02 - CARE™ Response to COVID-19

Review and Canadian perspectives provided by CARE™ Oncology Faculty member:

Dr. Barbara Melosky
BC Cancer (BC)
Osimertinib as adjuvant therapy in patients (pts) with stage IB–IIIA EGFR mutation positive (EGFRm) NSCLC after complete tumor resection: ADAURA.

Clinical trial information: NCT02511106.

Roy S. Herbst et al.

Osimertinib is a 3rd-generation, CNS-active, EGFR-TKI with superior efficacy to comparator EGFR-TKI (gefitinib/erlotinib) in treatment-naive EGFRm advanced NSCLC.

ADAURA is a Phase III, double-blind, randomized study assessing the efficacy and safety of osimertinib vs placebo (PBO) in pts with stage IB–IIIA EGFRm NSCLC after complete tumor resection and adjuvant chemotherapy, when indicated.

In stage II–IIIA patients, disease free survival (DFS) hazard ratio (HR) was 0.17 (95% CI 0.12, 0.23); p<0.0001 (156/470 events); 2-year DFS rate was 90% with osimertinib vs 44% with PBO.

In the overall population, DFS HR was 0.21 (0.16, 0.28); p<0.0001 (196/682 events); 2-year DFS rate was 89% with osimertinib vs 53% with PBO.

Overall Survival results are immature (4% maturity) with 29/682 deaths (osimertinib n=9, PBO n=20) at data cutoff.

The safety profile was consistent with the known safety profile of osimertinib, with mild EGFR TKI class effects reported.

<table>
<thead>
<tr>
<th>DFS by Stage</th>
<th>Stage IB</th>
<th>Stage II</th>
<th>Stage IIIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 year DFS rate, % (95% CI)</td>
<td>87 (77, 93)</td>
<td>91 (82, 95)</td>
<td>88 (79, 94)</td>
</tr>
<tr>
<td>Osimertinib</td>
<td>73 (62, 81)</td>
<td>56 (45, 65)</td>
<td>32 (23, 42)</td>
</tr>
<tr>
<td>Placebo</td>
<td>Overall HR (95% CI)</td>
<td>0.50 (0.25, 0.96)</td>
<td>0.17 (0.08, 0.31)</td>
</tr>
</tbody>
</table>

Study Conclusion:
Adjuvant osimertinib is the 1st targeted agent in a global trial to show a statistically significant and clinically meaningful improvement in DFS in patients with stage IB/II/IIIA EGFRm NSCLC after complete tumor resection and adjuvant chemotherapy. Adjuvant osimertinib provides an effective new treatment strategy for these patients.
**ASCO 2020 Abstract 9005. CTONG1104: Adjuvant gefitinib (G) versus chemotherapy (C) for resected N1-N2 NSCLC with EGFR mutation—Final overall survival analysis of the randomized phase III trial 1 analysis of the randomized phase III trial.**

Clinical trial information: NCT01405079

Yi-Long Wu et al.

**Trial Background/Summary:**
- ADJUVANT-CTONG1104, a randomized phase 3 trial showed adjuvant gefitinib treatment significantly improved disease-free survival (DFS) vs standard doublet chemotherapy in patients with epidermal growth factor receptor (EGFR) mutation-positive resected stage II-IIIA (N1-N2) non-small-cell lung cancer (NSCLC).
  - Final overall survival (OS) results from the study were presented (median follow-up was 76.9 months).
  - Median OS (mOS) was 75.5 months based on 95 (42.8%) events in the ITT whole population.
  - mOS was 75.5m in the G arm, and 79.2m in C arm (HR 0.96, 95%CI 0.64-1.43, p=0.823).
  - Subsequent treatment (especially targeted therapy) contributed most to OS (HR = 0.46, 95% CI 0.26 – 0.83).
  - The RR was 26.7%, DCR 66.7%, mPFS 14.1m and mOS 19.6m for patients rechallenged with an EGFR TKI in the G arm (n=15).

**Study Conclusion:**

The DFS survival advantage did not translate to OS difference in ADJUVANT trial.

**ASCO 2020 Abstract 9504. Trastuzumab deruxtecan (T-DXd; DS-8201) in patients with HER2-mutated metastatic non-small cell lung cancer (NSCLC): Interim results of DESTINY-Lung01.**

Clinical trial information: NCT03505710.

Egbert F. Smit et al.

**Trial Background/Summary:**
- T-DXd is an antibody-drug conjugate composed of an anti-HER2 antibody, cleavable tetrapeptide-based linker, and topoisomerase I inhibitor payload. In a phase I trial, patients (pts) with HER2-mutated NSCLC who received T-DXd had a confirmed objective response rate (ORR) of 72.7% (8/11) (Tsurutani et al, WCLC 2018).
  - Data was reported for the cohort with HER2 mutations after a median follow-up of 8.0 mo (range, 1.4-14.2 mo).
  - Median treatment duration was 7.75 mo (range, 0.7-14.3 mo); 45.2% of pts remained on treatment.
  - Confirmed ORR by ICR among the 42 pts was 61.9% (95% CI, 45.6%-76.4%); median DOR was not reached at data cutoff; 16 of 26 responders remained on treatment at data cutoff; DCR was 90.5% (95% CI, 77.4%-97.3%); estimated median PFS was 14.0 mo (95% CI, 6.4-14.0 mo).
  - All pts (42/42) had treatment-emergent adverse events (TEAEs); 64.3% were grade ≥ 3 (52.4% drug-related), including decreased neutrophil count (26.2%) and anemia (16.7%).
  - TEAEs led to dose interruption in 25 pts (59.5%), dose reduction in 16 pts (38.1%), and treatment discontinuation in 10 pts (23.8%).

**Study Conclusion:**

T-DXd demonstrated promising clinical activity with high ORR and durable responses in pts with HER2-mutated NSCLC.
ASCO 2020 Abstract 9506. NEJ026: Final overall survival analysis of bevacizumab plus erlotinib treatment for NSCLC patients harboring activating EGFR-mutations.

Clinical trial information: UMIN000017069.

Trial Background/Summary:

- In NEJ026, a phase III trial comparing bevacizumab plus erlotinib (BE) to erlotinib monotherapy (E) for EGFR-mutated non-small-cell lung cancer (NSCLC), progression-free survival (PFS) of BE was significantly superior to E (Saito et al. Lancet Oncol. 2019 May;20(5):625-635.)
- For the follow-up OS analysis, median follow up time was 39.2 months.
- Median OS was 50.7 months (95% CI, 37.3 months to not reached) with BE and 46.2 months (95% CI, 38.2 months to not reached) with E (hazard ratio, 1.00; 95% CI, 0.68 to 1.48).
- The median survival time between enrollment and progressive disease of second-line treatment (median PFS2) was 28.6 months (95% CI, 22.1 months to 35.9) with BE and 24.3 months (95% CI, 20.4 months to 29.1 months) with E (hazard ratio, 0.80; 95% CI, 0.59 to 1.10).

Study Conclusion:
The additional effect of bevacizumab on erlotinib monotherapy for NSCLC with EGFR mutations did not lead to an overall survival difference.


Results from several clinical trials that investigated novel MET research and drug development in lung cancer where presented during the clinical science symposium, MET Mutations: The Meat of the Matter. What follows is a snapshot of the trials presented during the symposium with additional background drawn from presentations made by the session chair and discussants, Drs. Ravi Salgia, Timothy F. Burns, and Laura Mezquita.

Background on MET:

Timeline of MET

- MET RTK inhibitors are active against MET Ex14 alterations.
- MET amplifications are reported in 1-6% of patients with NSCLC.
- MET RTK inhibitors are active against MET Ex14 alterations.
Resistance mechanisms arise with MET RTK inhibition.

- The frequency and type of resistance may change.
- Combination therapies may be beneficial to present or overcome resistance.
- Has cancer MET its match? Yes, but there is still work to do!
  - More potent and diverse classes of MET targeting agents may improve outcomes further.

**MET Trials Presented:**

**ASCO 2020 Abstract 9505.** Capmatinib in patients with high-level MET-amplified advanced non–small cell lung cancer (NSCLC): results from the phase 2 GEOMETRY mono-1 study.

Clinical trial information: NCT02414139.

*Juergen Wolf et al.*

**Study Conclusion:**

Capmatinib has demonstrated activity in the subset of pts with high-level MET-amplified (GCNs≥10) NSCLC, with a higher response rate in treatment-naive pts. Safety profile remains favorable and similar to previous reports of capmatinib.
**ASCO 2020 Abstract 9511.** Characterization of 1,387 NSCLCs with MET exon 14 (METex14) skipping alterations (SA) and potential acquired resistance (AR) mechanisms.

*Mark M. Awad*

**Study Conclusion:**

In a dataset of > 60,000 advanced NSCLCs, METex14 SA were present in 2.3% of cases, and represented 6 major subtypes. Among paired cases, potential AR mechanisms included secondary MET alts (33%), and acquired alts in EGFR, ERBB2, KRAS, and PI3K pathways. Acquired alts were independent of the type of METex14 SA. Characterizing common co-occurring may be critical for predicting responses to MET inhibitors and informing rational combination strategies.


*D. Ross Camidge et al.*

**Study Conclusion:**

Sym015 was well-tolerated at the RP2D with a response rate similar to MET TKI in MET-treatment naïve MET↑ Amp/Ex14∆ NSCLC and seems to delay disease progression in MET TKI pretreated NSCLC pts. Combination with MET TKI to delay or prevent resistance should be further explored.
A study was conducted with the aim of better understanding the reality of treatment and approaches to education during the current COVID-19 pandemic with consideration of the near-term future (<2 years).

On May 4th, 2020, a survey was emailed and/or mailed to oncologists across Canada. The 10-item survey covered 3 areas: approaches related to delivery of therapy in clinic; near-term impact on patient outcome, and clinician education/knowledge transfer.

**Key Takeaways:**

**Demographics of Survey Respondents**
Response to date is 62 (18%), with responses from clinicians working in academic and community centres across all regions of Canada.

**Approaches and needs related to delivery of therapy at clinic**
- 71% of respondents agree that their patient’s access to clinic has decreased, with 92% indicating that in the near term (<2 years) approaches to clinic will NOT return to pre-COVID period of care.
- With respect to value of sharing of experiences and approaches across centres, 72% indicate guidance is needed.

**Impact on patient outcome**
- 93% of responders indicate that impact on patient outcomes in the near-term (<2 years) is not fully understood. Clinicians are considering a variety of options to safely treat patients in clinic. 92% of respondents agree that approaches to clinic will not return to pre-COVID period clinic and 93% indicate that these approaches to treatment will need to re-evaluate.
- 78% of responders suggest changes will become institutionalized and 66% consider these as not optimal for patient outcome.

**Approaches for clinician education in near-term (<2 years)**
- While 78% of clinicians indicate that national and international congresses provide the highest yield in terms of education value; in the near-term, 82% suggest on-line education will become their preferred method of knowledge transfer.

**Conclusions/Follow-up actions:**

There is an expressed need for clear guidance on approaches to treatment in the near term. Guidance should consider impact on patient outcomes before becoming institutionalized at either regional or national level.

Interest in learning continues but has shifted online. This interaction, while having less perceived yield versus national and international congresses, may serve in the near-term to connect oncologists to address education needs and knowledge transfer.

As a follow-up participating CARE™ faculty are planning virtual meetings with colleagues from across the country. The aim of this collaboration is to share approaches for patient care and safety at clinic in the absence of an effective vaccine for COVID-19. Considerations to be discussed include, but are not limited to: how to manage patient load given the backlog of testing and/or patient visits caused by COVID; timing of referral and treatment initiation (i.e. longer-term planning and considers for patients who require escalation sooner); evolving priorities and impact of treatment decisions in COVID era (i.e. oral vs. infusion, risks with immunocompromising patients, etc.).

This national guidance of best practices will acknowledge needs of institution size and regional considerations. Timing for delivery is Fall 2020.
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