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Event Summary

Thank you for joining us at our recent Best of ASCO® Toronto Conference. Here is your exclusive summary of the event's most compelling trial reviews. This content was developed in consultation with the conference Chairs.

NADINA • ESOPEC • LAURA • PALOMA-3 • DESTINY-Breast06

Study #1 - NADINA

Neoadjuvant nivolumab plus ipilimumab versus adjuvant nivolumab in macroscopic, resectable stage III melanoma: The phase 3 **NADINA** trial.

Summary of key data:

1. Results of the phase III NADINA trial support **a new standard of care for the treatment of resectable macroscopic stage III melanoma**.
2. Treatment with preoperative ipilimumab plus nivolumab followed by total lymph node dissection, with adjuvant therapy guided by depth of response, led to a highly significant 68% relative reduction in the risk of disease recurrence or death as compared to standard-of-care dissection and adjuvant nivolumab.
3. Significantly fewer events occurred in the neoadjuvant arm (combination of ipilimumab + nivolumab) vs the adjuvant arm (28 vs 72), with HR 0.32 (99.9% CI, 0.15 to 0.66, p<0.0001) and estimated 12-month event-free survival (EFS) rates of 83.7% (99.9% CI, 73.8 to 94.8) vs 57.2% (99.9% CI, 45.1 to 72.6) favoring the neoadjuvant arm.
4. All subgroups benefit from neoadjuvant ipilimumab + nivolumab. In the BRAFmut melanoma subgroup, estimated EFS rates were 83.5% and 52.1%, and in the BRAFwt subgroup, 83.9% and 62.4% for neoadjuvant vs adjuvant respectively.
5. Of the 59% of patients achieving a major pathologic response, some were able to avoid adjuvant therapy altogether, limiting their total treatment time to 6 weeks.

Study #2 - ESOPEC

Prospective randomized multicenter phase III trial comparing perioperative chemotherapy (FLOT protocol) to neoadjuvant chemoradiation (CROSS protocol) in patients with adenocarcinoma of the esophagus (**ESOPEC** trial).

Summary of key data:

1. Perioperative FLOT improves overall survival (OS) in resectable esophageal adenocarcinoma compared to neoadjuvant CROSS (HR 0.70, 95% CI, 0.53 to 0.92, p=0.012); median follow-up 55 months
    a. FLOT: median OS, 66 (95% CI, 36 to not estimable) months; 3-year OS rate, 57.4% (95% CI, 50.1 to 64.0%); 5-year OS rate, 50.6%.
    b. CROSS: median OS, 37 (95% CI, 28 to 43) months; 3-year OS rate, 50.7% (95% CI, 43.5 to 57.5%); 5-year OS rate, 38.7%.
2. In 359 patients with available tumor regression status, pathologic complete response was achieved in 19.3% (95% CI, 13.9 to 25.9%) in the FLOT arm and 13.5% (95% CI, 8.8 to 19.4%) in the CROSS arm.
3. FLOT is better than CROSS in gastroesophageal adenocarcinoma patients; however, CROSS underperformed in this study as 67.7% completed pre-op treatment vs 87.7% for FLOT.
4. **CROSS alone is no longer standard of care**; adjuvant immunotherapy is indicated for patients with non-pathological complete response.

Study #3 - LAURA

Osimertinib (OSI) after definitive chemoradiotherapy (CRT) in patients (PTS) with unresectable stage (STG) III epidermal growth factor receptor-mutated (EGFRm) NSCLC: Primary results of the phase 3 **LAURA** study.

Summary of key data:

1. **Osimertinib** (n=143) **significantly improved progression-free survival** (PFS) vs placebo (n=73): HR 0.16; 95% CI, 0.10 to 0.24; p<0.001; median PFS, 39.1 vs 5.6 months; 12-month PFS rate, 74% vs 22%; 24-month PFS rate, 65% vs 13%; PFS benefit seen across subgroups.
2. Interim overall survival (OS) analysis (20% maturity) favored osimertinib: HR 0.81; 95% CI, 0.42 to 1.56; p=0.530; 81% of patients in the placebo arm received osimertinib after progression.
3. Fewer patients with new lesions (22% vs 68% with placebo) and reduced progression in the brain (8% vs 29%) and lung (6% vs 29%) were reported in the osimertinib arm.
4. Safety results were expected and manageable. The most common adverse events were radiation pneumonitis (48% with osimertinib vs. 38% with placebo, majority Grade 1/2), diarrhea (36% vs. 14%), and rash (24% vs. 14%); higher rates of COVID-19 were also reported with osimertinib (20% vs 8%).
5. These **results establish osimertinib as the new standard of care for EGFRm NSCLC** in this setting.

Study #4 - PALOMA-3

Subcutaneous amivantamab vs intravenous amivantamab, both in combination with lazertinib, in refractory EGFR-mutated, advanced non-small cell lung cancer: Primary results, including overall survival, from the global, phase 3, randomized controlled **PALOMA-3** trial.

Summary of key data:

1. Subcutaneous (SC) amivantamab + lazertinib (n=206) demonstrated noninferior pharmacokinetics, objective response rate and median time to response (1.5 months in both arms) compared to IV amivantamab + lazertinib (n=212).
2. SC amivantamab was associated with:
    a. Numerically longer median duration of response (DoR; 11.2 months with SC vs 8.3 months with IV among confirmed responders) and progression-free survival (PFS; median, 6.1 vs 4.3 mo; HR, 0.84; p= 0.20).
    b. Significantly improved overall survival (OS): HR, 0.62; 95% CI, 0.42 to 0.92; nominal p=0.017); 12-month OS rate, 65% vs 51% for IV.
    c. Fewer rates of infusion-related reactions (IRRs, 13% with SC vs 66% with IV, primarily grade 1-2) and venous thromboembolism (VTE; all patients, 9% vs 14% with IV; on prophylactic anticoagulation, 7% vs 12%; no prophylactic anticoagulation, 17% vs 26%).
    d. Reduced treatment administration time (median <5 min vs 2-5 hours with IV).
    e. Higher rates of patient-reported convenience at cycle 1 day 1 (85% vs 52% with IV, p < 0.001) and at end of treatment (85% vs 35%, p <0.001).
3. Severe bleeding risk was low among all patients receiving anticoagulants (1% grade ≥3).

Study #5 - DESTINY-Breast06

Trastuzumab deruxtecan vs physician's choice of chemotherapy in patients with hormone receptor–positive, human epidermal growth factor receptor 2 (HER2)–low or HER2-ultralow metastatic breast cancer with prior endocrine therapy: primary results from DESTINY-Breast06.

Summary of key data:

1. For **patients with HER2-low cancer** (n=713), **T-DXd** (n=359) **significantly improved progression-free survival** (PFS) vs chemotherapy (n=354): HR, 0.62 [95% CI, 0.51 to 0.74], p<0.0001; median PFS, 13.2 vs 8.1 months.
2. PFS benefit with T-DXd was seen in HER-2 ultralow group (n=153; HR, 0.78 [95% CI, 0.50 to 1.21]; median PFS, 13.2 vs 8.3 months) although not statistically significant;
    - HER-2 ultralow population requires further clarification on testing criteria and confirmation with larger sample size/data maturity.
3. OS was immature at first interim analysis: HER-2 low (HR, 0.83 [95% CI, 0.66 to 1.05], p=0.1181); HER-2 ultralow groups (HR, 0.75 [95% CI, 0.43 to 1.29]; 12-month OS rate, 84.0% vs 78.7%); median follow up, 18.6 months.
4. T-DXd safety concerns include higher rates of interstitial lung disease/pneumonitis (11.3% vs 0.2% with chemotherapy; most common cause of treatment discontinuation [5.3%]), cardiac dysfunction (8.1% vs 2.9%), alopecia (45%), treatment-related deaths (5 vs 0), grade ≥3 treatment-related adverse events (TEAE, 40.6% vs 31.4%).
    - Nausea was the most common TEAE associated with dose reduction (4.4%).
5. These results solidify the role of T-DXd in HER-2 low population with evidence of efficacy in chemotherapy-naive mBC settingwas 14.3% for T-DXd vs 9.4% for chemotherapy. Pneumonitis was the most common TEAE associated with treatment discontinuation for T-DXd (5.3%).

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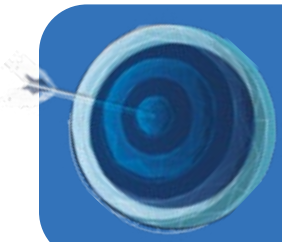

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Chairs: Dr. Heather McArthur & Dr. Sumanta Pal

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