HIGHLIGHTS FROM GICS 2017

Members of the CARE Gastrointestinal Cancer Faculty recently attended the Gastrointestinal Cancers Symposium (GICS) 2017 conference held in San Francisco, CA from January 19-21.

The CARE Perspectives Conference Report from GICS 2017 provides a summary of the most compelling stories and news presented at this event, and is augmented with additional perspectives from the CARE Gastrointestinal Cancer Faculty.

CARE GASTROINTESTINAL CANCER FACULTY WHO HAVE CONTRIBUTED TO THIS REPORT:

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The content that follows is written in the language in which it was presented and is adapted from the abstracts from the GICS 2017 conference. Perspectives are provided by the CARE Gastrointestinal Cancer Faculty.
GICS 2017. Abstract 303: Efficacy and safety of liposomal irinotecan (nal-IRI) + 5-fluorouracil and leucovorin (5-FU/LV) in patients (pts) with metastatic pancreatic ductal adenocarcinoma (mPDAC) who previously received gemcitabine (gem)-based therapy: Post-hoc analysis of the NAPOLI-1 trial
Li-Tzong Chen et al.

Results: Of 117 pts in the nal-IRI+5-FU/LV arm, 53 (45%) previously received gem monotherapy and 64 (55%) previously received gem combo including erlotinib (n = 9) or nab-paclitaxel (n = 20). Of the 119 pts in the 5-FU/LV arm, 55 (46%) previously received gem monotherapy and 64 (54%) previously received gem combo including erlotinib (n = 17) or nab-paclitaxel (n = 11). Nal-IRI+5-FU/LV improved median OS, median PFS, and ORR vs 5-FU/LV, regardless of prior therapy (Table). Grade ≥3 treatment-emergent adverse events were not influenced by prior treatment. Clinical trial information: NCT01494506

OS, PFS, ORR Results

<table>
<thead>
<tr>
<th></th>
<th>Gem Mono</th>
<th>Gem Combo</th>
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<tbody>
<tr>
<td></td>
<td>Nal-IRI+</td>
<td>Nal-IRI+</td>
</tr>
<tr>
<td></td>
<td>5-FU/LV</td>
<td>5-FU/LV</td>
</tr>
<tr>
<td>n</td>
<td>53</td>
<td>64</td>
</tr>
<tr>
<td>OS, months, median (95% CI)</td>
<td>7.1 (4.6-10.2)</td>
<td>6.1 (4.6-8.4)</td>
</tr>
<tr>
<td>P</td>
<td>0.31</td>
<td>0.06</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.81 (0.54-1.22)</td>
<td>0.7 (0.49-1.02)</td>
</tr>
<tr>
<td>PFS, months, median (95% CI)</td>
<td>4.3 (3.4-6.1)</td>
<td>4.2 (2.7-5.8)</td>
</tr>
<tr>
<td>P</td>
<td>0.03</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.63 (0.41-0.96)</td>
<td>0.54 (0.36-0.81)</td>
</tr>
<tr>
<td>ORR</td>
<td>15%</td>
<td>19%</td>
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<tr>
<td>Efficacy by prior gem-based regimen</td>
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</table>

Conclusions: These results show consistent benefit of nal-IRI+5-FU/LV treatment across subgroups of pts who previously received gem therapy and support the ASCO guidelines recommending nal-IRI+5-FU/LV for this pt population. These analyses may be limited by the small sample size of treatment arms.

CARE FACULTY PERSPECTIVE:
Gemcitabine containing regimens, either as a single agent or in combination with nab-paclitaxel remain appropriate treatment options in Canada for first line treatment of patients with pancreatic cancer. In particular, combination therapy has demonstrated improved overall survival and QoL in appropriately selected patients resulting in its adoption as one of the gold-standard therapies for first line treatment. Moreover, it appears that first line treatment with a gemcitabine containing combination regimen may also be a predictor of receiving second line therapy thus potentially leading to improved outcomes.

However, despite the recent advances in the management of advanced cancers, patients with pancreatic cancer continue to have relatively few therapeutic options in the second line setting and have generally poor outcomes. This type of data is certainly encouraging and demonstrates that the addition of liposomal irinotecan to infusional 5FU/LV improves both PFS and OS vs 5FU/LV alone. It should be noted however, that the comparator chemotherapy arm was not our typical standard and was different from that used in the experimental arm. In addition, given the population at hand, it would have been ideal to have a group managed with palliative care alone to further highlight the likelihood of treatment effect.

This trial highlighted the importance of first line therapy in the probability of receiving second line therapy and thus achieving an OS benefit. It will be interesting to see how payers will interpret this data given that in Ontario, the non-liposomal irinotecan-containing regimen FOLFIRI is not considered evidenced-informed for this indication and is not yet reimbursed.

THIS TYPE OF DATA IS CERTAINLY ENCOURAGING AND DEMONSTRATES THAT THE ADDITION OF LIPOSOMAL IRINOTECA TO INFUSIONAL 5FU/LV IMPROVES BOTH PFS AND OS VS 5FU/LV ALONE.
GICS 2017. Abstract 293. Characteristics of Long-term Survivors in a Randomized Phase 3 Trial (NAPOLI-I) of Patients With Metastatic Pancreatic Ductal Adenocarcinoma (mPDAC) Treated With Liposomal Irinotecan (nal-IRI; MM-398) + 5-FU/LV

Andrea Wang-Gillam et al.

Results: A total of 29 (25%) pts in the nal-IRI+5-FU/LV arm and 17 (14%) in the 5-FU/LV arm survived ≥ 1 year. These pts typically had better performance status, lower CA19-9 (U/mL) levels, and were less likely to have liver metastases at baseline, compared with the overall population. For long-term survivors in the nal-IRI+5-FU/LV arm, a higher proportion of pts had neutrophil-to-lymphocyte ratio (NLR) >5, a marker of poor prognosis, suggesting that higher NLR may potentially be predictive of survival outcome with nal-IRI+5-FU/LV.

Conclusions: More pts receiving nal-IRI+5-FU/LV versus 5-FU/LV were alive beyond 1 year. The most prominent prognostic markers of survival ≥ 1 year included lower CA19-9, KPS ≥ 90 and absence of liver metastases. These analyses may be limited by small sample sizes. Clinical trial information:NCT01494506

CARE FACULTY PERSPECTIVE:
This analysis, although limited by its small sample size, identifies that there may be potential predictors of outcome that we still need to elucidate. It is generally accepted that for patients with pancreatic cancer, good performance status accurately identifies patients more likely to both receive, and experience meaningful benefit from, therapy compared to those with poorer performance status. In addition, this analysis should be put into context with previous findings that patients receiving gemcitabine combination therapy were both more likely to receive second line treatment and have an improvement in overall survival compared to those patients that received only single agent gemcitabine. There is also evidence from these trials that suggest that a reduction in CA19-9 with first line therapy is associated with better outcomes. Thus, whether the findings presented are reflective of the results from the first line therapy or prognostic prior to second line treatment is somewhat unclear and will require further study and validation.


Keisuke Kazama et al.

Results: A total of 221 patients were evaluated in the study. The overall complication rates are 44.8% in Group A and 52.6% in Group B. Surgical mortality was observed in 2 patients due to an abdominal abscess and cardiovascular disease in Group A (1.1%) and in 1 patient due to postoperative bleeding in Group B (2.6%). There were no significant differences (p=0.379 and p=0.456, respectively). Furthermore, the 5-year OS and RFS rates were similar between the elderly patients and non-elderly patients (18.55% vs. 20.2%, p=0.946 and 13.1% vs. 16.0%, p=0.829 respectively).

Conclusions: The short-term outcomes and long-term outcomes survival after pancreatic resection for pancreatic adenocarcinoma were almost equal in the elderly and the non-elderly patients in this study. Therefore, it is unnecessary to avoid pancreatic resection for pancreatic adenocarcinoma in elderly patients simply because of their age.

CARE FACULTY PERSPECTIVE:
This study highlights a key element of cancer treatment that has been shown many times across multiple tumour types and treatment indications – chronological age is not a definitive predictor of patient outcome and should not be used to exclude appropriate patients from potentially beneficial therapy. Rather, appropriate assessment of functional age and careful patient selection are much more important for decision-making. In addition, it is important to remember that in order to increase the likelihood of success with a minimum of morbidity and mortality, the treatment of these patients should be restricted to high volume centres with surgical teams experienced with managing patients undergoing a Whipple’s procedure.

PATIENTS RECEIVING GEMCITABINE COMBINATION THERAPY WERE BOTH MORE LIKELY TO RECEIVE SECOND LINE TREATMENT AND HAVE AN IMPROVEMENT IN OVERALL SURVIVAL COMPARED TO THOSE PATIENTS THAT RECEIVED ONLY SINGLE AGENT GEMCITABINE.
COLORECTAL CANCER
THE COMMENTARY PROVIDED IN THE COLORECTAL CANCER SECTION IS PROVIDED BY DR. SHARLENE GILL.

GICS 2017. Abstract 519: Nivolumab alone or in combination with ipilimumab in patients with DNA mismatch repair deficient/microsatellite instability high metastatic colorectal cancer: Updated results from CheckMate 142.

Michael J. Overman et al.

Results: Among pts treated with nivo 3 Q2W (N = 74), 84% had received ≥ 2 prior lines of therapy. ORRs were 31% (INV) and 27% (IRRC); disease control rates were 69% (INV) and 62% (IRRC). The median time to response was ≈ 2.7 mo (INV/IRRC). PFS rates at 12 mo were 48.4% (INV) and 45.6% (IRRC). The duration of response and OS medians were not yet reached; OS rates were 83.4% (6 mo) and 73.8% (12 mo). Responses were observed in pts regardless of tumour programmed death-1 ligand 1 (PD-L1) expression level or BRAF or KRAS mutation status and were observed in pts with or without a history of Lynch syndrome (Table). Grade 3–4 treatment-related adverse events (TRAEs) occurred in 20% of pts. TRAEs leading to discontinuation included acute kidney injury, increased ALT, colitis, and stomatitis (1 each). No treatment-related deaths occurred in this arm.

ORR Results

<table>
<thead>
<tr>
<th>Tumour PD-L1 expression</th>
<th>Nivo 3 Q2W</th>
</tr>
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<tbody>
<tr>
<td>&lt;1%</td>
<td>11/45; 24%</td>
</tr>
<tr>
<td>≥1%</td>
<td>7/21; 33%</td>
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</table>

<table>
<thead>
<tr>
<th>Mutation status</th>
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<tbody>
<tr>
<td>BRAF mutant</td>
<td>2/12; 17%</td>
</tr>
<tr>
<td>KRAS mutant</td>
<td>6/26; 23%</td>
</tr>
<tr>
<td>BRAF/KRAS wild type</td>
<td>9/28; 32%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lynch syndrome (clinical history)</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Yes</td>
<td>8/23; 35%</td>
</tr>
<tr>
<td>No</td>
<td>6/26; 23%</td>
</tr>
</tbody>
</table>

ORRs in biomarker-defined populations per IRRC:

Conclusions: Nivo showed durable responses and disease control in heavily pretreated pts with dMMR/MSI-H mCRC. Treatment was well tolerated, with no new safety signals. Clinical trial information: NCT02060188

GICS 2017. Abstract 658: CHARTA: FOLFOX+bevacizumab +/- irinotecan in advanced colorectal cancer (CRC)—Final results of the randomized phase II trial of the AIO (KRK 0209).

Hans-Joachim Schmoll et al.

Results: Evaluable 241 pts. (1 not elig., 8 prot. violation); m/f: 65%/35%, age 61 yrs. (21-82), left/right: left A: 51, 5%, B: 48, 5%; right A: 45%, B: 55%; ECOG 0-1/2: 96% / 4%, ESMO-group 1/2/3: 29%/ 55%/ 16%. Primary endpoint was met: significantly improved PFS at 9 months 56% vs. 68% (p= 0.086). Preliminary PFS 9.7 vs. 12.0 months (HR 0.77, p=0.61), identical to TRIBE: 9.7 vs. 12.1. Response (A/B): CR: 5/5%, CR/PR 60/70%, SD 25/21%, PD 14/9%; sec. resection: 21/23%. Subgroup - analyses did not show significant differences, except CR / PR left/right (A/B): left 59/68%, right 63/73%; PFS (months) left 10.4/12 (HR 0.69, p=0.03), right: 8.2 /10.7; non-significant improvement in ESMO-group 3 (HR 0.51), RAS-wt (HR 0.67), Koehne-Score High risk HR 0.58; ECOG1: HR 0.69. QL-Global=Health-Score: slightly worse in A, vs. improved in B. Dose-intensity <70%/ 70-90%/ >90% (A/B): 39/37%/ 18/26%/ 41/36%; initial dose-reduction 17% of pts. Toxicity: low to moderate without major differences between A & B, except grade 3 diarrhea 12/16%, neutrophils 14/20%, GI 12/20%.

Conclusions: The 4-drug-regimen has superior activity with the same outcome as TRIBE and is well tolerated, without a negative effect of initial dose-reduction, and an improvement of global QoL-Score. Clinical trial information: NCT01321957

CARE FACULTY PERSPECTIVE:
The previously reported TRIBE study demonstrated the survival superiority of FOLFOXIRI-bev versus FOLFIRI-bev in untreated mCRC (Loupakis, NEJM 2014:371). This study used FOLFOX/bev as the standard arm comparator with an updated PFS improvement from 10 mos to 12 months (p=0.097 with significance predefined at p<0.1) yet similar OS (27.8 mos versus 24.8 mos, p=0.95). While this study was underpowered for survival, the benefit of a first-line 4-drug regimen is less clear with FOLFOX/bev as the standard comparator. A meta-analysis is planned.
GICS 2017. Abstract 520: Randomized phase II study of irinotecan and cetuximab with or without vemurafenib in BRAF-mutant metastatic colorectal cancer (SWOG 1406).

Scott Kopetz et al.

Results: 106 patients were enrolled (54 in the experimental arm) from 12/2014 to 4/2016, with ECOG PS ≤ 1. Median age of 62 years, 59% female, and prior irinotecan therapy in 39%. PFS was improved with the addition of vemurafenib (HR = 0.42, 95% confidence interval [CI] of 0.26 to 0.66, P < 0.001) with median PFS of 4.4 (95% CI: 3.6 – 5.7) months vs 2.0 (95% CI: 1.8 – 2.1). Response rate was 16% vs 4% (P = 0.09), with disease control rate of 67% vs 22% (P < 0.001). Grade 3/4 adverse events higher in the experimental arm included neutropenia (28% vs 7%), anemia (13% vs 0%), and nausea (15% vs 0%). There was no increase in skin toxicity or fatigue. No new safety signal was observed. Approximately 50% of patients in the control arm crossed over at the time of progression. Overall survival and efficacy at cross-over data remain immature.

Conclusions: The addition of vemurafenib to the combination of cetuximab and irinotecan resulted in a prolongation of progression-free survival and a higher disease control rate, indicating that simultaneous EGFR and BRAF inhibition is effective in BRAF V600 mutated CRC. Clinical trial information: NCT02164916

CARE FACULTY PERSPECTIVE:

The estimated 7% of patients with mCRC tumours that harbour a BRAF mutation are known to have a very poor prognosis, particularly after failure of first-line therapy. The HR of 0.42 (p=0.0002) for PFS favouring the vemurafenib containing arm (with a disease control rate of 67%) is encouraging, and validated the preclinical data that vemurafenib sensitizes BRAFm disease to cetuximab and irinotecan. This study was also notable as it confirmed the feasibility of conducting randomized trials in small molecular subsets of CRC. While a phase 3 study is not planned given the poor prognosis of these patients, further maturity of the OS data (despite crossover) will be needed to determine the clinical utility and value of vemurafenib in this setting. In addition, further analyses by MSI status are pending as there is significant overlap in this population and immune checkpoint therapy has emerged as a preferred strategy for MSI-H pretreated mCRC.

“THIS STUDY WAS ALSO NOTABLE AS IT CONFIRMED THE FEASIBILITY OF CONDUCTING RANDOMIZED TRIALS IN SMALL MOLECULAR SUBSETS OF CRC.”
GASTRIC/GASTRO-ESOPHAGEAL CANCER

THE COMMENTARY PROVIDED IN THE GASTRIC/GASTRO-ESOPHAGEAL CANCER SECTION IS PROVIDED BY DR. SHARLENE GILL.

GICS 2017. Abstract 2: Nivolumab (ONO-4538/BMS-936558) as salvage treatment after 2nd or later line chemotherapy for advanced gastric or gastro-esophageal junction cancer (AGC): A double-blinded, randomized phase III trial.

Yoon-Koo Kang et al.

Results: As of the data cut-off on Aug 13th 2016, 5.6 months after last patient randomized, median OS was 5.32 months with nivolumab versus 4.14 months with placebo (hazard ratio [HR], 0.63; 95% confidence interval [CI], 0.50-0.78; p<0.0001), and OS rates at 6 and 12 month were 46.4% versus 34.7% and 26.6% versus 10.9%, respectively. The overall response rate (ORR) was 11.2% (95% CI, 7.7-15.6) with nivolumab versus 0% (95% CI, 0.0-2.8) with placebo (p<0.0001). Median progression-free survival (PFS) was 1.61 months with nivolumab versus 1.45 months with placebo (HR, 0.60; 95% CI, 0.49-0.75; p<0.0001). Grade ≥3 drug-related adverse events (AEs) occurred in 11.5% of nivolumab and 5.5% of placebo; 2.7% and 2.5%, respectively, discontinued of study treatment due to drug-related AEs (any grade).

Conclusions: Nivolumab was effective as the salvage treatment for pretreated AGC with significantly improved OS, PFS and ORR compared to placebo. Clinical trial information: NCT02267343

CARE FACULTY PERSPECTIVE:
This phase 3 trial aimed to evaluate the safety and efficacy of nivolumab as a salvage treatment after standard chemotherapy for patients with advanced gastric or gastro-esophageal junction cancer. This follows on the heels of earlier phase II studies with PD-1 inhibitors in pre-treated disease (including KEYNOTE 12 with pembrolizumab, and Checkmate 32 with nivolumab.) While the median survivals do not appear significantly impressive, the HR is the more interpretable endpoint with I-O therapies and, in this case, a HR of 0.63 with a 1-year survival of 27% vs 11% seems meaningful. The limitation is that this is in an Asian only population and no biomarker data was presented. It would be reasonable to await other phase 3 checkpoint inhibitor studies in this space such as JAVELIN 300 (avelumab, PD-L1) and await biomarker analyses to better understand which patients with pre-treated gastric and GEJ cancers are most likely to benefit from an immunotherapy approach.

“IT WOULD BE REASONABLE TO AWAIT OTHER PHASE 3 CHECKPOINT INHIBITOR STUDIES AND AWAIT BIOMARKER ANALYSES TO BETTER UNDERSTAND WHICH PATIENTS ARE MOST LIKELY TO BENEFIT FROM AN IMMUNOTHERAPY APPROACH.”
GICS 2017. Abstract 4: A randomized, double-blind, multicenter phase III study evaluating paclitaxel with and without RAD001 in patients with gastric cancer who have progressed after therapy with a fluoropyrimidine/platinum-containing regimen (RADPAC).

Salah-Eddin Al-Batran et al.

Results: 300 patients (median age: 62 years; median lines prior therapy: 2) were randomly assigned (Arm A, 150; Arm B, 150). Response rate (complete and partial response) was 8.0% (95% CI: 4.2%-13.6%) in the paclitaxel/RAD001 arm and 7.3% (95% CI: 3.7%-12.7%) in the paclitaxel/placebo arm (p = 0.4). There was no significant difference in median PFS (placebo, 2.07 vs. RAD001, 2.2 months, HR 0.88, p = 0.3) and median OS (placebo, 5.1 vs. RAD001, 6.1 months, HR 0.92, p = 0.48). Combination of paclitaxel and RAD001 was tolerable, but the placebo arm was associated with significantly less (any grade) mucositis (15.8% vs. 37.2%), fever (10.3% vs 20.7%), leukopenia (11.6% vs. 21.4%), neutropenia (13.0% vs. 27.6%) and thrombocytopenia (2.1% vs 14.5%).

Conclusions: The addition of RAD001 to paclitaxel/RAD001 did not significantly improve outcomes in pretreated metastatic gastric or esophagogastric junction adenocarcinoma. Additional biomarker studies are planned to look for subgroups that may have a benefit. Clinical trial information: NCT01248403


Kazumasa Fujitani et al.

Results: 104 pts, 71 males and 33 females with a median age of 68 years, were enrolled. The types of surgery were DG in 23 pts, TG in 9 pts, GJS in 70 in pts, and exploratory laparotomy in 2 pts. Baseline QOL questionnaires were completed by 103 (99.0%) pts. Among the 104 pts, 98 (94.2%), 100 (96.1%), and 81 (77.9%) completed the 2-wk, 1-m, and 3-m follow-up survey, respectively. The mean baseline EQ-5D score was 0.74 (SD, 0.21). During the follow-up period, the mean scores remained consistent with the baseline scores; the change from baseline score was within ± 0.05 for the index. Many pts came to eat solid food at 2 wks post-surgery and remained tolerable thereafter (from 0 at baseline to 82, 85, 75 pts at 2 wks, 1 m, and 3 ms, respectively). Overall morbidity rate of ≥ grade 3 on Clavien-Dindo classification and 30-day postoperative mortality rate was 9.6% (10 pts) and 2.0% (2 pts) with a median hospital stay of 13 days and re-operation rate of 3.9% (4 pts).

Conclusions: In pts with malignant GOO caused by advanced GC, surgical palliation maintained patient QOL while improving solid food intake with an acceptable surgical safety. Clinical trial information: UMIN000023494.
GICS 2017. Abstract 225: Gemox versus surveillance following surgery of localized biliary tract cancer: Results of the PRODIGE 12-ACCORD 18 (UNICANCER GI) phase III trial.
Julien Edeline et al.

Results: Between July 2009 and February 2014, 196 patients were included in 33 French centers. Baseline characteristics were balanced, with similar primary sites, RO resection rates were 86.2% (Arm A) vs 87.9% (Arm B), lymph node invasion present in 37.2% vs 36.4%. In Arm A, a median of 12 cycles was delivered (mean: 9.3, range: 0-12). Maximal grade of adverse events were grade 3 in 57.5% vs 22.2%, and grade 4 in 17.0% vs 9.1%. During treatment one patient died in each arm. The main grade ≥3 adverse events in the year following inclusion were peripheral neuropathy (50.0% vs 1.1%), and neutropenia (22.3% vs 0%). Median follow-up was 44.3 months, with 54 and 64 RFS events in arms A vs B. There was no significant difference in RFS between the arms (log-rank p = 0.31), with a hazard ratio of 0.83 [95% CI: 0.58-1.19], p = 0.31 (futility boundaries were crossed). Median RFS was 30.4 [95% CI: 15.4-45.8] vs 22.0 months [95%CI: 13.6-38.3] in arms A & B respectively, and 4-years RFS was 39.3% [95%CI: 28.4%-50.0%] vs 33.2% [95%CI: 23.1-43.7%]. Global Health HrQoL scores were not different at 12 months (70.8 vs 83.3, p = 0.18) and at 24 months (75.0 vs 83.3, p = 0.50).

Conclusions: Adjuvant chemotherapy in BTC with GEMOX was feasible and associated with expected toxicities and no deterioration of HrQoL. There was no significant difference in RFS between GEMOX and surveillance. Clinical trial information: NCT01313377

CARE FACULTY PERSPECTIVE:
Adjuvant therapy for patients with fully resected gallbladder and cholangiocarcinomas remains somewhat of a grey area. Despite the benefit of gemcitabine and platinum-containing regimens in the treatment of advanced disease, there is currently no accepted standard in patients post surgery performed with curative intent. This study showed that the combination of gemcitabine and oxaliplatin did not result in a statistically significant improvement in RFS compared to active surveillance and was, as one might expect, associated with significant toxicities including half of patients experiencing a grade 3 sensory neuropathy. While this study doesn’t advance our ability to offer patients effective adjuvant therapy, it does highlight the fact that the prognosis of these patients is generally fairly good.

Ignacio Melero et al.

Results: Across dose escalation and expansion phases, 262 patients have been treated. Grade 3/4 treatment-related adverse events occurred in 20%. No maximum tolerated dose was reached during dose escalation (n = 48). The ORR (investigator-assessed) was 20% (95% CI 15-26) in 214 patients treated in the dose expansion phase with a median DoR of 9.9 months; DCR was 64% (95% CI 58-71). Responses were observed across etiologies and regardless of tumor PD-L1 expression. ORRs of 23% (95% CI 13-36) and 21% (95% CI 11-34) were observed in the uninfected sorafenib-naive and -treated patients, respectively. The 9-month overall survival rate in the expansion phase was 74% (95% CI 67-79). Association between immune-cell biomarkers and clinical outcomes will be presented.

Conclusions: In this heavily pretreated population, responses to nivolumab were durable with encouraging overall survival. Safety was manageable and consistent with that observed in other solid tumors with no new safety signals. Clinical trial information: NCT01658878

CARE FACULTY PERSPECTIVE:
Advanced HCC is associated with few treatment options and a very poor prognosis. However, there is some emerging evidence to suggest that novel approaches with immunomodulating therapy is beneficial in this population. Previously, oncolytic viruses have shown some promise. Now, this study has demonstrated the benefit of another immuno-oncology approach with PD-1 inhibition. Adverse events were as expected and there were no new safety signals even in the patients with prior hepatitis infection. An interesting finding here was the lack of response association with PDL-1 status. The survival data although somewhat modest is still encouraging and warrants additional investigation.

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