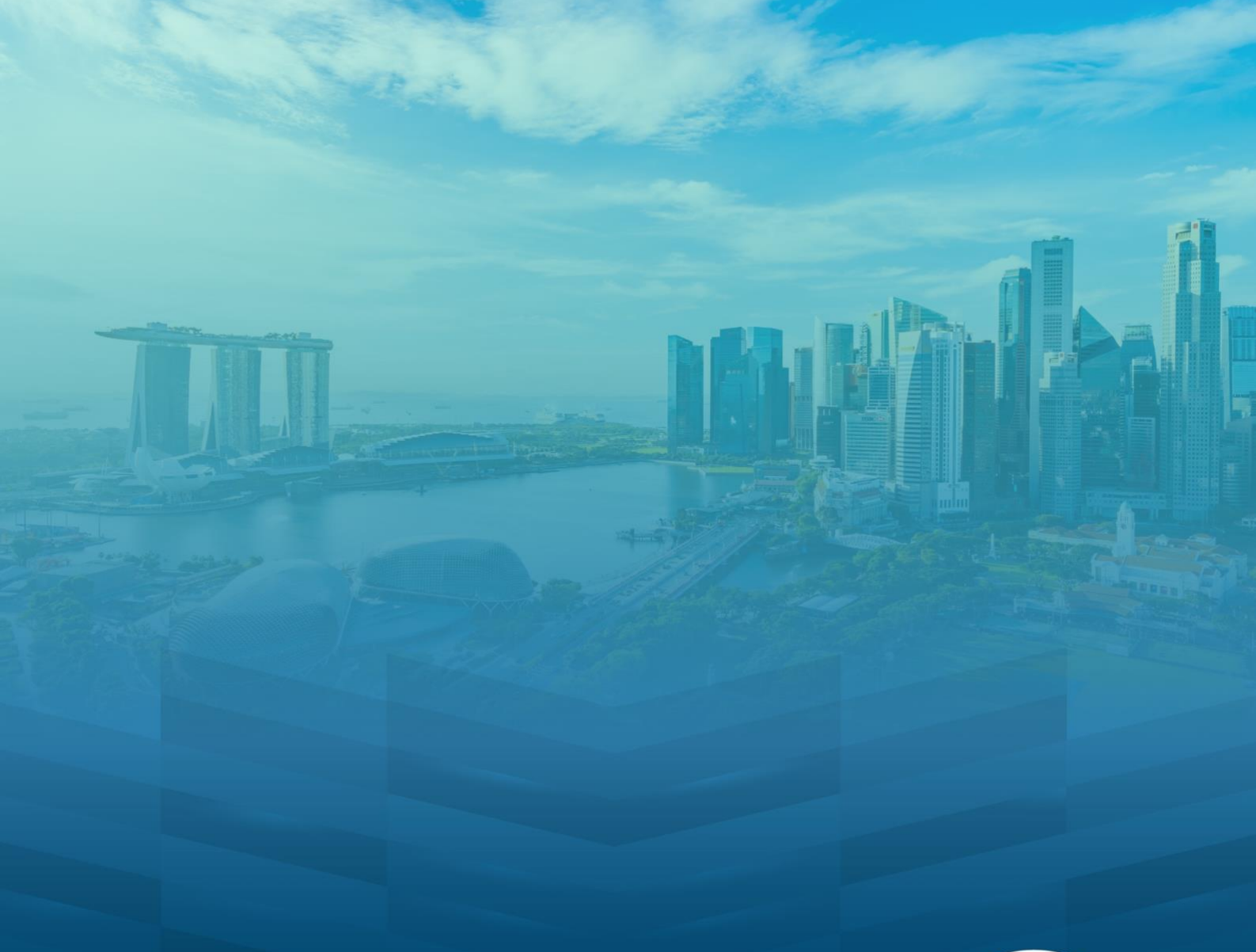

Singapore Society of Oncology

7th Annual Scientific Meeting

8 - 9 July 2022 | Virtual Meeting

ABSTRACTS

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Index

Category : Biomarkers (BMK)

ID : BMK 1

Name : Chun Chau Lawrence Cheung

Organisation : Singapore General Hospital

Title

Immunohistochemical scoring of LAG-3 in conjunction with CD8 in the tumor microenvironment predicts responses to immune checkpoint blockade immunotherapy in hepatocellular carcinoma

Introduction

Hepatocellular carcinoma (HCC) is the sixth most frequently diagnosed cancer and the third leading cause of cancer-related mortalities. Immune checkpoint blockade (ICB) is a systemic therapeutic option for advanced HCC. However, low response rates amongst patients necessitate the development of robust predictive biomarkers that can identify individuals who would benefit from ICB. Previously, our group found that immunohistochemical scoring of CD38 in the tumor microenvironment predicted responses to anti-PD-1/anti-PD-L1 immunotherapy in HCC patients. A 4-gene inflammatory signature, comprising CD8, PD-L1, LAG-3, and STAT1, was recently shown to be associated with a better overall response to immunotherapy in various cancer types. In the present study, we examined whether tissue protein expression of CD8, PD-L1, LAG-3, and STAT1 predicts responses to ICB in HCC.

Methods

HCC tissue samples from 191 Asian patients, including resection specimens from 124 patients (ICB-naïve) and pre-treatment specimens from 67 advanced HCC patients treated with ICB (ICB-treated), were analyzed for CD8, PD-L1, LAG-3, STAT1, CD38, and CD68 tissue expression using multiplex immunohistochemistry followed by survival and statistical analyses.

Results

Immunohistochemical and survival analyses of ICB-naïve patients showed that high LAG-3 expression was associated with shorter median progression-free survival (mPFS) and overall survival (mOS). Analysis of ICB-treated samples revealed that high pre-treatment LAG-3+ and LAG-3+CD8+ cell proportions were most closely associated with longer mPFS and mOS. Moreover, levels of CD8, STAT1, CD38, and CD38+CD68+, but not PD-L1, were significantly correlated with better responses to ICB. Using a log-likelihood model, adding the total LAG-3+ or LAG-3+CD8+ cell proportions to the total CD8+ cell proportion significantly increased the predictive values for PFS and OS, compared with total CD8+ cell proportion alone. After separately analyzing viral-related and non-viral HCC samples, only the LAG3+CD8+ cell proportion was significantly associated with responses to ICB regardless of etiology.

Conclusion

High pre-treatment LAG3 and CD8 protein expression in the tumor microenvironment predicted responses to ICB in HCC patients, regardless of viral status. Immunohistochemical scoring of pre-treatment expression levels of LAG-3 in conjunction with CD8 may help predict ICB benefits in HCC patients, using readily available and translatable immunohistochemistry-based techniques in the clinical setting.

This abstract submission :

This is an encore abstract.

Category : Breast Cancer (BRC)

ID : BRC 1

First Name : Divya Dahiya

Organisation : PGIMER, Chandigarh

Title

Quality of life assessment after breast cancer treatment using EORTC QLQ-C30 and BR23 questionnaire: a prospective study from a tertiary care centre in north India

Introduction

Breast cancer is the most common type of cancer among women globally. Measuring quality of life in breast cancer patients is of importance in assessing treatment outcomes. This study examined the impact of breast cancer treatment on quality of life.

Methods

This was a prospective study of quality of life in breast cancer patients following completion of treatment which includes surgery, chemotherapy and radiation therapy. Quality of life was measured using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and its breast cancer supplementary measure (QLQ-BR23) at three points in time: three months, one year and two years after completion of treatment. Total 56 patients were enrolled in the study by using purposive sampling technique. Socio-demographic and clinical data included: age, education, marital status, disease stage and initial treatment. Repeated measure analysis was performed to compare quality of life differences over the time.

Results

The mean age of breast cancer patients was 46.9±10.1years and majority (82%) underwent mastectomy along with chemo and radiotherapy. The results showed there were significant differences in patients' functioning and global quality of life at three points in time (p <0.001). Although there were deteriorations in patients' scores for body image and sexual enjoyment, there were significant improvement for breast symptoms and systemic therapy side effects (p < 0.05). In functioning scale; physical, cognitive, emotional, social and role functioning improved. However, in symptoms scale, fatigue was the most common problem experienced by the patients even after 2 years of surgery followed by financial difficulties and arm symptoms.

Conclusion

Overall quality of life has been improved globally after breast cancer treatment from 3 months to 2 years. However, fatigue and arm symptoms need supportive treatment on follow up.

This abstract submission :

This is an encore abstract.

Category : Breast Cancer (BRC)

ID : BRC 2

First Name : Denise Goh

Organisation : A*STAR

Title

Early triple negative breast cancers in a Singapore cohort exhibit high PIK3CA mutation rates associated with low PD-L1 expression

Introduction

Triple negative breast cancer (TNBC) is known to be one of the most aggressive and heterogeneous forms of breast cancer associated with a poor prognosis. In recent years, mutations in the PI3K pathway, particularly of PIK3CA, were reported to be intimately associated with disease progression and the development of resistance to current treatments. Multiple PI3K pathway inhibitors have entered the clinic, albeit with contradictory results. PIK3CA mutations in the context of the immune landscape in TNBC remain poorly defined.

Methods

We performed genomic profiling of PIK3CA and other genes on 166 women with early-stage TNBC from Singapore General Hospital, for comparison to publicly available TNBC cohorts (FUSCC, TCGA and METABRIC: 276 Chinese TNBCs, 129 non-Asian TNBCs, and 292 European TNBCs). These tumors were profiled transcriptionally using a Nanostring panel of immune genes and using multiplex immunohistochemistry. We further manually scored the tissue for PD-L1-positivity using two clinically relevant clones, SP142 and 22C3.

Results

We discovered a higher rate of PIK3CA mutations in our Singapore TNBC cohort as compared to non-Asian TNBC patients, along with TP53, BRCA1, PTPN11, and MAP3K1 alterations. PIK3CA mutations did not affect overall or recurrence-free survival, and when compared to PIK3CAWT tumors, there were no differences in immune infiltration. Using two clinically approved antibodies, PIK3CAmut tumors were associated with PD-L1 negativity. Analysis of co-mutation frequencies further revealed that PIK3CA mutations tended to be accompanied by mutations in the MAP kinase pathway.

Conclusion

A higher prevalence of PIK3CA mutations was observed in Singapore early-stage TNBCs. The mechanism and impact of PIK3CA alterations on the TNBC tumor immune microenvironment and PD-L1 positivity warrant further study.

Category : Gastrointestinal Tumors (GIT)

ID : GIT 1

First Name : Ryan Yong Kiat Tay

Organisation : National University of Singapore

Title

Choice of PD-L1 immunohistochemistry assay influences clinical eligibility for gastric cancer immunotherapy

Introduction

Immune checkpoint inhibitors (ICI) are now standard-of-care treatment for patients with metastatic gastric cancer (GC). To guide patient selection for ICI therapy, programmed death ligand-1 (PD-L1) biomarker expression is routinely assessed via immunohistochemistry (IHC). Regulatory approval for ICIs is granted based on PD-L1 expression status, scored using metrics such as the combined positive score (CPS). However, with an increasing number of approved ICIs, each paired with a different PD-L1 antibody IHC assay used in their respective landmark trials, there is an unmet clinical and logistical need for harmonization. We thus investigated the interchangeability between the Dako 22C3, Dako 28-8 and Ventana SP-142 assays in GC PD-L1 IHC.

Methods

In this cross-sectional study, samples were obtained via biopsy or resection of gastric cancer at the National University Hospital, Singapore. We scored 362 GC samples for PD-L1 CPS, tumor proportion score (TPS) and immune cells (IC) using a multiplex immunohistochemistry/immunofluorescence technique. 344 samples were developed into a tissue microarray (TMA), while 18 samples were used as whole slides for orthogonal validation. The samples selected for whole slide analysis were obtained from GC patients treated with ICI therapy.

Results

The percentage of PD-L1 positive samples at clinically relevant CPS ⩾1, ⩾5 and ⩾10 cut-offs for the 28-8 assay were approximately two-fold higher than that of the 22C3 (CPS⩾1: 70.3% vs 49.4%, p<0.001; CPS⩾5: 29.1% vs 13.4%, p<0.001; CPS⩾10: 13.7% vs 7.0%, p=0.004). The mean CPS score on 28-8 assay was nearly double that of the 22C3 (6.39 ±14.5 vs 3.46±8.98, p<0.001). At the clinically important CPS⩾5 cut-off, there was only moderate concordance between the 22C3 and 28-8 assays.

Conclusion

Our findings suggest that scoring PD-L1 CPS with the 28-8 assay may result in higher proportion of PD-L1 positivity and higher PD-L1 scores compared to assessment with the 22C3 and other assays. Our multiplex IHC samples showed that two PD-L1 antibodies appear to bind to different parts of the PD-L1 protein, causing different cells to show as positive. This may explain the discrepancies between the assays. Clinically, this could lead to a larger number of patients eligible and approved for ICI therapy. As such, until stronger evidence of inter-assay concordance is found, we urge caution in treating the assays as equivalent.

This abstract submission :

This is an encore abstract.

Category : Gastrointestinal Tumors (GIT)

ID : GIT 2

First Name : Seng Wee Cheo

Organisation : National University Hospital

Title

Ciprofloxacin plus Gemcitabine-based Chemotherapy in Patients with Metastatic Pancreatic Ductal Adenocarcinoma – A Pilot Study of Microbiome Manipulation

Introduction

Gemcitabine-based chemotherapy is an approved therapy for treatment-naïve metastatic pancreatic ductal adenocarcinoma (PDAC). Inherent resistance to gemcitabine inevitably leads to cancer progression and shorter survival. It has been demonstrated that bacteria are a component of the PDAC tumor microenvironment and may play a critical role in mediating resistance to chemotherapy. Hence, the coadministration of an antibiotic to chemotherapy may potentiate antitumour drug responses. We conducted a pilot study to assess the efficacy and safety of ciprofloxacin plus gemcitabine-based chemotherapy in patients with treatment naïve metastatic PDAC. We also aimed to study gut microbiome changes during treatment with ciprofloxacin.

Methods

This was a single arm study conducted at the National University Cancer Institute, Singapore. Patients (pts) with histologically confirmed metastatic PDAC were treated with nab-paclitaxel (125 mg/m2) and gemcitabine (1000 mg/m2) on days 1, 8, and 15 every 4 weeks, in combination with oral ciprofloxacin 500 mg twice daily. Treatment was continued until disease progression or intolerable toxicity. DNA extraction, 16S rRNA amplification and sequencing for bacteria were performed on pre- and post-treatment stool samples. Primary endpoint of this study was response rate and safety of the treatment combination. Secondary endpoints included progression free survival (PFS), overall survival (OS) and microbiome changes after treatment with ciprofloxacin.

Results

From Mar 2019 - Feb 2021, 8 pts were recruited. Median age was 71 years old. Best response was stable disease in 5 (62.5%) pts and 3 pts had progressive disease (PD). Median PFS and OS were 4.3 and 15.4 months, respectively. 2 pts developed grade 4 neutropenia and 1 pt had grade 3 febrile neutropenia. Rash was common with 50% of pts developed grade 1/2 rash. No additional toxicities from ciprofloxacin were observed. Preliminary stool analysis showed significant differences in individual bacterial strains across all timepoints in the PD vs. SD groups. There was also an increased abundance in gammaproteobacteria resistant to ciprofloxacin treatment in pts with PD.

Conclusion

Gemcitabine-based chemotherapy plus ciprofloxacin demonstrated clinical activity and acceptable safety profile in PDAC. Our study also highlighted that gut microbiome may play a critical role in mediating resistance to chemotherapy.

This abstract submission :

This is an encore abstract.

Category : Gastrointestinal Tumors (GIT)

ID : GIT 3

First Name : Elroy Saldanha

Organisation : Manipal Comprehensive Cancer Center Bangalore India

Title

PROSPECTIVE ANALYSIS OF IMPACT OF LEARNING CURVE IN ROBOTIC ASSISTED RECTAL SURGEY IN THE HIGH VOLUME INDIAN TERTIARY CARE CENTER

Introduction

Minimal invasive surgery in rectal cancer has gained prominence owing to its various advantages in surgical outcomes. Due to rapid adoption of robotics in rectal surgery, we intended to assess the pace in which surgeons gain proficiency using cumulation summation(CUSUM) technique in learning curve.

Methods

Prospective study of 262 rectal cancer cases undergoing Robotic assisted Low Anterior Resection and Abdomino-Perineal Resection (RA-LAR and RA-APR) were included with parameters like console time, docking time, lymph nodal yield, total operative time and post-operative outcomes were considered for the study. We used Manipal technique of port placements and modified centro-side docking for the procedure.

Results

Mean age of our study was 46.62 +/- 5.7 years, BMI 31.51 +/- 3.2 kg/m2, with 215(82.06%) underwent RA-LAR and 47 (17.93%) underwent RA-APR. 2.67% cases required to open during our initial period. We had three phases of learning curve, initial phase (11th case), plateau phase (29th case) and then phases of mastery (30th case onwards). Our mean total operative time reduced from 5.5 hours to 3.5 hours (210 +/- 8.2 mins), console time from 4.5 hours to 2.9 hours (174 +/- 4.5 mins) and docking time from 15 to 9 +/- 1 mins from 30th case onwards.

Conclusion

Robotic assisted surgeries for rectal cancer has got good oncological and functional outcomes in high BMI, male pelvis and low rectal cancers. Learning curve can be shortened with constant self auditing of the surgeon and team with each surgeries performed, reviewing the steps and by improvising techniques

This abstract submission :

This is an encore abstract.

Category : Gastrointestinal Tumors (GIT)

ID : GIT 4

First Name : Elroy Saldanha

Organisation : Manipal Comprehensive Cancer Bangalore India

Title

A Prospective Analysis of 168 cases of Robotic 3-stage Esophagectomy for Carcinoma Esophagus in a Tertiary Care Cancer Centre

Introduction

Esophageal cancer is the eighth most common cancer in the world and the sixth most common cause of cancer death. Esophagectomy with locoregional lymphadenectomy is the standard treatment of patients with resectable esophageal neoplasm. Esophagectomy is a technically demanding operation. Robotic-assisted minimally invasive esophagectomy (RAMIE) is an alternative to standard minimally invasive esophagectomy (MIE), and has been increasingly applied to the treatment of esophageal cancer. This study aims to evaluate the safety and technical feasibility of Total Robot-Assisted Three-Stage Esophagectomy and to analyse short term oncological outcomes.

Methods

From November 2011 to November 2020, one hundred sixty-eight histologically proven (T1–4a, N+, M0) Resectable Carcinoma Esophagus patients with ECOG performance status of 0 and 1, who underwent Robot-Assisted Transthoracic and Transabdominal Three-Stage Esophagectomy. We aimed to evaluate the safety and technical feasibility of Total Robot-Assisted Three-Stage Esophagectomy. Technique and feasibility of robot assisted surgery in terms of operating time, estimated blood loss, total number of lymph nodes retrieved, postoperative ventilator support, ICU stay, hospital stay, conversion to open procedure, margin status (mucosal and circumferential), intraoperative and postoperative complications were analysed. We used ICG for identification of thoracic duct intra-operatively. Complications were classified according to Modified Clavien–Dindo classification (MCDC) of surgical complications.

Results

One hundred sixty-eight total robotic esophagectomies were performed. All the patients presented in stage III and were subjected to NACT with TPF regimen. Post NACT, a partial response of 58.8% was achieved and 17.6% patients achieved a complete response. Total docking time for initial ten cases was 67.90 ± 13.24 minutes, while for subsequent cases it was 33.20 ± 4.16 minutes similarly total operative time was 429.20 ±57.65min & 321.13 ±13.75min for initial ten cases and subsequent cases, thoracic-phase operative time for initial ten cases and subsequent cases was 96.60 ±20.33minutes and 57.04 ±9.15minutes showing the steeper learning curve in robotics which is in contrast to minimal access surgery. The average blood loss was 280.32 ± 17.52 ml. Incidence of vocal cord palsy was 4.8% while delayed gastric emptying was noted in 3.2% of population. In postoperative period two patients required ventilator support, twenty patients needed ICU stay rest were shifted directly to wards, Pneumonia was reported in 1% of patients, anastomotic leak in 2.8% of patients which was managed conservatively. With the longest follow up of 50 months, 3-year DFS and OS was 75.4% & 68% respectively.

Conclusion

Robotic-assisted esophagectomy has an advantage of total thoracic and abdominal minimally invasive surgery with very low conversion rates, short learning curve, excellent chance of good quality lymphadenectomy in supra-azygous and bilateral recurrent laryngeal nerve area option for both robotic stapler and handsewn intracorporeal anastomosis with limitations of the need for specific teaching programs and proctored learning, both of which are mandatory. Total robotic esophagectomy is technically feasible in terms of completeness of surgery, achieving adequate margins and nodal harvest with minimal pulmonary morbidities.

This abstract submission :

This is an encore abstract.

Category : Genitourinary Tumors (GUT)

ID : GUT 1

First Name : Anuradha Krishnan

Organisation : Tata Memorial Hospital

Title

Trimodality therapy for bladder cancer: Initial experience of moving from conventional to hypo-fractionation

Introduction

Traditionally, bladder preserving Chemoradiation for invasive bladder cancer is treated by conventionally fractionated radiotherapy (Conv-RT) to 64Gy. A recent meta-analysis reported the non- inferiority with moderately hypofractionated schedule (Hypo-RT) of 55Gy in 20 fractions. In light of this evidence, we changed our practice from Conv-RT to Hypo-RT. We present our initial experience on acute toxicity and challenges related to concomitant chemotherapy and pelvic irradiation with Hypo-RT.

Methods

Consecutive patients from a prospectively maintained institutional database with biopsy proven, non-metastatic, high-grade urothelial bladder cancer with clinical stage T2-T3, N0-N1 treated with Hypo-RT between December 2021 to April 2022 were analysed. A similar cohort of consecutive patients treated with Conv-RT between January 2018 to November 2021 were included as the historical cohort. All patients were treated with adaptive plan-of-the-day radiotherapy (ART) with daily image guidance and IMRT technique. Patients in Hypo RT cohort received 55Gy in 20 fractions over 4 weeks and 44Gy to the pelvis. In Conv RT cohort, patients received 64Gy over 32 fractions over 6.5 weeks and 55Gy to the pelvis. Patients were reviewed weekly while on RT, at conclusion and thereafter 3 monthly along with cystoscopy. Acute toxicity, defined as toxicity during the course of RT up to a period of 3 months post RT, was assessed using the RTOG and CTCAE criteria. Details regarding neoadjuvant, concurrent chemotherapy and target volumes were analysed in both cohorts.

Results

A total of 76 patients were included with 36 patients in the Hypo-RT cohort and 40 patients in the Conv-RT group. 30% in Hypo-RT and 40% of patients in Conv-RT cohort received NACT and 80% received concurrent gemcitabine or cisplatin in each of the cohorts. The target volume included regional pelvic nodes in 80% patients in each cohort. There was no significant difference between Hypo-RT and Conv-RT with respect to acute grade 2 genitourinary (GU) toxicity (14% vs 15%, p= 0.78). Acute grade 2 gastrointestinal (GI) toxicity (16.7% vs 5%, p = 0.18) was higher with Hypo-RT. There were no grade 3-4 toxicities with either of the two schedules. Acute grade 2 GU toxicity experienced with Hypo-RT schedule was dysuria in all 5 patients, while with Conv-RT 4 patients had dysuria, 1 had incontinence and 1 had haematuria. Acute grade 2 GI toxicity with Hypo-RT was diarrhoea in 5 patients and rectal pain in 1 patient. Both the patients who experienced acute grade 2 GI toxicity in Conv-RT cohort had diarrhoea. Toxicity related early termination or major treatment breaks (>7 days) occurred in 4 patients in Conv-RT cohort and 1 patient in Hypo-RT cohort.

Conclusion

Hypo-RT was well tolerated and can be safely used for bladder preservation along with concomitant chemotherapy and pelvic irradiation in patients with bladder cancer. Hypo-RT schedule had modestly increased and mostly self-limiting grade 2 acute GI toxicity compared to Conv-RT.

Category : Genitourinary Tumors (GUT)

ID : GUT 2

First Name : See-Tong Pang

Organisation : Chang Gung Memorial Hospital

Title

Overall survival of patients with metastatic hormone-sensitive prostate cancer in the phase 3 ARASENS study of darolutamide versus placebo in combination with androgen-deprivation therapy and docetaxel

Introduction

Darolutamide is a structurally distinct and highly potent androgen receptor inhibitor with demonstrated efficacy and safety in patients with nonmetastatic castration-resistant prostate cancer. In patients with metastatic hormone-sensitive prostate cancer (mHSPC), the addition of docetaxel to androgen-deprivation therapy (ADT) has been shown to improve overall survival (OS). The ARASENS trial (NCT02799602) evaluated the effect of darolutamide in combination with ADT and docetaxel on OS in patients with mHSPC.

Methods

In this international, double-blind, phase 3 trial, patients with mHSPC were randomized 1:1 to darolutamide 600 mg or placebo twice daily plus ADT and docetaxel. Randomization was stratified by extent of metastatic disease (nonregional lymph node metastases only [M1a]; bone ± lymph node metastases [M1b]; visceral ± lymph node/bone metastases [M1c]) and alkaline phosphatase (ALP) level (< or ⩾ upper limit of normal at study entry). The primary endpoint was OS and key secondary efficacy endpoints included time to castration-resistant prostate cancer (CRPC), pain progression, first symptomatic skeletal event (SSE), and first subsequent antineoplastic therapy. Safety was assessed by treatment-emergent adverse events (TEAEs).

Results

Between November 2016 and June 2018, 1306 patients were randomized to darolutamide (n=651) or placebo (n=655) and 1305 patients (n=651 and 654, respectively) were included in the full analysis set. Baseline characteristics were generally balanced between treatment groups. At the primary analysis (data cutoff October 25, 2021), darolutamide significantly decreased the risk of death by 32.5% versus placebo (HR 0.68; 95% CI 0.57–0.80; P<0.001). The significant improvement in OS was observed despite the finding that more patients in the placebo group received subsequent life-prolonging systemic therapy versus the darolutamide group (75.6% vs 56.8%). The significant OS benefit was consistent across subgroups. Darolutamide also significantly delayed time to CRPC versus placebo (HR 0.36; 95% CI 0.30–0.42; P<0.001), time to pain progression (HR 0.79; 95% CI 0.66–0.95; P=0.01), time to first SSE (HR 0.71; 95% CI 0.54–0.94; P=0.02), and time to first subsequent antineoplastic therapy (HR 0.39; 95% CI 0.33–0.46; P<0.001). The incidences of TEAEs were similar between treatment groups, and incidences of the most common TEAEs (⩾10%) were highest during the overlapping docetaxel treatment period in both groups. Grade 3/4 TEAEs occurred in 66.1% of darolutamide patients and 63.5% of placebo patients, mainly due to neutropenia (grouped term; 33.7% vs 34.2%). Discontinuations of study drug due to TEAEs occurred in 13.5% of patients receiving darolutamide and 10.6% of patients receiving placebo.

Conclusion

In patients with mHSPC, early treatment intensification with darolutamide plus ADT and docetaxel significantly improved OS compared with ADT and docetaxel alone. Darolutamide also significantly delayed the time to key secondary efficacy endpoints, including CRPC. The safety profile of darolutamide was consistent with previous reports and darolutamide did not increase adverse events associated with ADT and docetaxel.

This abstract submission :

This is an encore abstract.

Category : Gynecological Tumors (GYT)

ID : GYT 1

First Name : Kush Shah

Organisation : Manipal Hospitals

Title

Aggressive Angiomyxoma of the vulva: A Rare Occurrence

Introduction

Background: Aggressive angiomyxoma is a rare, slow growing, soft and benign mesenchymal tumor that predominantly affect the perineum of women in reproductive age group. It is locally infiltrating and has a high risk of local recurrence.

Methods

We herein describe a case of a 30 years old female presenting with a recurrent polypoidal mass in left side of introitus and something coming down per vagina, measuring 5 x 3x 2cm and burning sensation while passing urine. Histopathologically, the lesion was composed of elongated spindle and stellate-shaped cells embedded in a myxoid stroma. Another specific feature was the presence of prominent component of thin to thick walled vessels with perivascular clustering plump epithelioid cells. The tumor was immunoreactive for vimentin, progesterone receptor (PR) and focally positive for estrogen receptor (ER). Patient underwent wide local excision of the tumor with clear margins and developed local recurrence after 2 years.

Results

Aggressive angiomyxoma of the vulva needs to be distinguished from benign myxoid tumors with low risk of local recurrence as well as from malignant myxoid neoplasms. Usually wide local excision with tumor free margins and occasionally hormonal manipulation is the treatment of choice.

Conclusion

Aggressive angiomyxoma of the vulva needs to be distinguished from benign myxoid tumors with low risk of local recurrence as well as from malignant myxoid neoplasms. Usually wide local excision with tumor free margins and occasionally hormonal manipulation is the treatment of choice.

Category : Gynecological Tumors (GYT)

ID : GYT 2

First Name : Elroy Saldanha

Organisation : Manipal Comprehensive Cancer Center Bangalore India

Title

NIPEC With Single Dose Intra-Peritoneal Cisplatin And Paclitaxel In Stage III Epithelial Ovarian Cancer

Introduction

Epithelial Ovarian Cancer is heterogeneous, essentially peritoneal disease. Standard treatment consists of staging, cytoreductive surgery and adjuvant chemotherapy. In this study, we intended to assess the effectiveness of single dose intra-peritoneal (IP) chemotherapy in optimally debulked advanced EOC patients.

Methods

Prospective randomized study of 87 patients with advanced EOC from January 2017 to May 2021 was done in our center. Patients underwent primary and interval cytoreduction received single dose of IP chemotherapy after being divided into four groups Group A – IP Cisplatin, Group B – IP Paclitaxel, Group C - IP Paclitaxel and Cisplatin, Group D –Saline for 24 hours. Pre and post peritoneal IP cytology was assessed along with possible complications.Logistic Regression analysis was used to assess for intergroup significance in cytology and complications. Kaplan-Meir analysis was done for DFS

Results

87 patients with FIGO stage III were in group A(cisplatin), 22(25.3%) patients in group B(paclitaxel), 23(26.4%) in group C(cisplatin and paclitaxel), 20(23%) in group D(saline). Cytology samples taken during staging laparotomy were positive and post-IP chemotherapy 48 hours, 2 (9%) samples of 22 in cisplatin group and 14 (70%) of 20 saline group samples were positive, rest of the post-IP group samples B and C were negative. No major morbidity was noted. In our study, DFS in saline group was 15 months while in IP chemotherapy group was 28 months and was statistically significant based log rank test. However, there was no significant difference in DFS between IP chemotherapy groups.

Conclusion

Complete or optimal CRS in advanced EOC does have a possibility of microscopic peritoneal residue. Adjuvant loco-regional strategies should be considered to prolong disease free survival. Single dose normothermic intraperitoneal chemotherapy can be offered to the patients with minimal morbidity and prognostic benefits comparable to HIPEC. Future clinical trials are required to validate these protocols.

This abstract submission :

This is an encore abstract.

Category : Gynecological Tumors (GYT)

ID : GYT 3

First Name : Elroy Saldanha

Organisation : Manipal Comprehensive Cancer Center Bangalore India

Title

SENTINEL NODE MAPPING USING INDOCYANINE GREEN AND NEAR-INFRARED FLUORESCENCE IMAGING TECHNOLOGY FOR ENDOMETRIAL CANCER: A PROSPECTIVE STUDY USING A SURGICAL ALGORITHM IN INDIAN PATIENTS

Introduction

Indocyanine Green(ICG) fluorescence with high definition 3D imaging systems is emerging as the latest strategy to improve surgical outcomes during Oncosurgery. It holds a great promise as a modern staging strategy for endometrial cancer. Aim was to assess the feasibility, diagnostic accuracy of SLN algorithm, evaluate the location and distribution of SLN and role of frozen section.

Methods

Prospective study involving 100 carcinoma endometrium patients who underwent robotic assisted type 1 pan hysterectomy, with ICG directed sentinel lymph node(SLN) biopsy from November 2020 to March 2022. SLN were sent for frozen section. Patients with positive sentinel nodes underwent complete lymph node dissection.

Results

Overall SLN detection rate was 98% with bilateral detection in 92% cases. Complete node dissection was done where SLN mapping failed. The most common location for SLN in our series was obturator on right and internal iliac on left hemiplevis. SLN in the para aortic area were detected in 14%. In 6% cases SLN were found at in atypical locations. 8% of patients had SLN positive for metastasis and underwent complete retroperitoneal lymphadenectomy. Comparison of final histopathology report with frozen section reports showed no false negatives.

Conclusion

ICG with cervical injection showed a high overall detection rate, and bilateral mapping appears to be a feasible alternative to the traditional methods of SLN mapping in patients with endometrial cancer. ICG fluorescence imaging system is simple, safe and may become a standard in oncosurgery. This approach can reduce morbidity, operative time, and costs associated with complete lymphadenectomy while maintaining prognostic & predictive information.

This abstract submission :

This is an encore abstract.

Category : Gynecological Tumors (GYT)

ID : GYT 4

First Name : Krishnansu S. Tewari

Organisation : University of California

Title

Pembrolizumab + chemotherapy in patients with persistent, recurrent, or metastatic cervical cancer: Subgroup analysis of KEYNOTE-826

Introduction

In KEYNOTE-826 (NCT03635567), pembrolizumab + chemotherapy ± bevacizumab provided statistically significant, clinically meaningful PFS and OS improvements in patients with persistent, recurrent, or metastatic cervical cancer. In the present analysis of KEYNOTE-826, we assessed outcomes in several key patient subgroups

Methods

Eligible adult patients had persistent, recurrent, or metastatic squamous cell carcinoma, adenosquamous carcinoma, or adenocarcinoma of the cervix not previously treated with chemotherapy and not amenable to curative treatment; measurable disease per RECIST v1.1; ECOG PS 0–1; and a tumor sample to determine PD-L1 status. Patients were randomized 1:1 to pembrolizumab 200 mg Q3W or placebo for up to 35 cycles + chemotherapy (paclitaxel 175 mg/m2 + cisplatin 50 mg/m2 or carboplatin AUC 5) ± bevacizumab 15 mg/kg. Dual primary endpoints were PFS by investigator assessment per RECIST v1.1 and OS in patients with PD-L1 CPS ≥1, all comers, and CPS ≥10. Treatment effects on PFS and OS were examined in patient subgroups defined by bevacizumab use (yes or no), histology (squamous or nonsquamous [including adenocarcinoma and adenosquamous]), platinum use (carboplatin or cisplatin), and prior chemoradiation therapy (CRT). Hazard ratios (HR) and 95% CIs were based on a stratified Cox regression model.

Results

617 patients were randomized (pembrolizumab + chemotherapy ± bevacizumab, n=308; placebo + chemotherapy ± bevacizumab, n=309). At the May 3, 2021 data cutoff, median follow-up was 22 months. In the all-comer population, pembrolizumab + chemotherapy prolonged median PFS compared with placebo + chemotherapy in all subgroups: with bevacizumab (15.2 versus 10.2 months; HR [95% CI], 0.61 [0.47–0.79]; n=389), without bevacizumab (6.3 versus 6.2 months; 0.74 [0.54–1.01]; n=228), squamous histology (10.4 versus 6.9 months; 0.63 [0.50–0.80]; n=447), nonsquamous histology (11.6 versus 8.4 months; 0.66 [0.43–1.00]; n=169), carboplatin use (10.2 versus 7.4 months; 0.69 [0.55–0.86]; n=495), cisplatin use (15.2 versus 8.4 months; 0.47 [0.28–0.77]; n=120), and prior CRT (10.3 versus 6.3 months; 0.62 [0.45–0.86]; n=243). Pembrolizumab + chemotherapy also prolonged median OS compared with placebo + chemotherapy in all subgroups: with bevacizumab (not reached [NR] versus 24.7 months; HR [95% CI], 0.63 [0.47–0.87]), without bevacizumab (16.8 versus 12.6 months; 0.74 [0.53–1.04]), squamous histology (23.5 versus 14.2 months; 0.61 [0.47–0.80]), nonsquamous histology (NR versus 21.3 months; 0.76 [0.47–1.23]), carboplatin use (21.4 versus 15.9 months; 0.69 [0.54–0.89]), cisplatin use (NR versus 21.3 months; 0.59 [0.32−1.09]), and prior CRT (21.3 versus 12.6 months; 0.64 [0.45−0.91]). Similar benefits of pembrolizumab + chemotherapy on PFS and OS were also seen in the protocol-specified CPS ⩾1 and CPS ⩾10 populations.

Conclusion

Pembrolizumab + chemotherapy ± bevacizumab prolonged PFS and OS versus placebo + chemotherapy ± bevacizumab among the subgroups defined by bevacizumab use, histology, platinum use, and prior CRT and provided clinically meaningful benefits similar to the broader population of patients with persistent, recurrent, or metastatic cervical cancer.

This abstract submission :

This is an encore abstract.

Category : Hematological Tumors (HMT)

ID : HMT 1

First Name : Djoko Agung Priyambodo

Organisation : ISHMO/ PERHOMPEDIN Indonesia

Title

EFFECTS OF CARBOGEN-NICOTINAMIDE INHALATION AND R-CHOP CHEMOTHERAPY ON P53 LEVELS IN DLBCL PATIENTS

Introduction

Inhalation of carbogen (95% oxygen / 5% carbon dioxide) and nicotinamide is said to improve intratumor oxygenation and improve post-therapy outcomes (radiotherapy and chemotherapy). This is evidenced in cancer patients who obtained improvements in gradient recalled echo (GRE) MRI results, sensitivity to changes in blood oxygenation and spin-echo (SE) MRI, and sensitivity to perfusion or blood flow is shown with a large increase in signal intensity. The tissue in the tumour has a hypoxia condition and the condition is associated with apoptosis, which is indicated by decreased p53 levels. DLBCL is the most common malignant of the lymph nodes where the therapy used is R-CHOP. However, 30% of cases do not respond to chemotherapy. This study aims to determine the effect of nicotinamide carbogen administration in DLBCL patients given RCHOP chemotherapy in a 1-time cycle against the apoptosis process.

Methods

Experimental, descriptive, and analytical research was conducted at dr Kariadi Hospital Indonesia. With a sample of 20 DLBCL patients. 10 patients with a diagnosis of DLBCL measured p53 levels were then given carbogen-nicotinamide inhalation and chemotherapy with the RCHOP regimen. Then measured p53 levels after administration of carbogen-nicotinamide inhalation and RCHOP. A control of 10 people with DLBCL measured p53 levels before chemotherapy (RCHOP) was carried out without carbogen-nicotinamide inhalation and repeated p53 measurements.

Results

The average age of the treatment group was 55.5 (24-61) while the control age was 58.5 (21-65) (p=0.307). The sexes in the treatment group were men 7 (70%) and women 3(30%), in the male control group 7(70%) and women 3(30%). The p53 level before the administration of carbogen-nicotinamide in the treatment group was 71.5 (14-601) after administering carbogen-nicotinamide to 145.8 (Â±131.37). There was an increase in p53 of 6.8 (Â±118.23). In the control group, the p53 levels before the administration of carbogen-nicotinamide were 236.5 (23-415), after the administration of carbogen-nicotinamide 157.6 (Â±124.27), there was a decrease of -65.3 (Â±138.7). Thus in the treatment group, there was an increase in p53 compared to the control group which decreased, although the changes between the two groups were not statistically meaningful (p = 0.839)

Conclusion

Carbogen-nicotinamide inhalation and R-CHOP were able to improve apoptosis, although changes between the two groups were meaningless.

Category : Head and Neck Cancers (HNC)

ID : HNC 1

First Name : Jingyi Ma

Organisation : DukeNUS Medical School

Title

The Tumour Immune Microenvironment of Recurrent/Metastatic NPC

Introduction

Nasopharyngeal carcinoma (NPC) is endemic in southern China and Southeast Asia. While the primary tumour can be treated with radiotherapy with or without chemotherapy, the management of recurrent/metastatic (RM) diseases remains a challenge. Over the last decade, targeted and immune therapies have emerged as promising treatment modalities for RM NPC. Particularly, anti-PD1 therapies have demonstrated encouraging effects against RM NPC in multiple clinical trials. However, PD-1-based therapies are limited by patient-specific responsiveness and adaptive resistance after long-term use. To improve the response rate, one approach is to introduce adjunct therapies targeting other dysregulated pathways in RM NPC. However, what contributes to the refractoriness of RM NPC remains to be elucidated.

Methods

In this study, we sought to characterise and compare features of tumour cells, tumour stroma and tumour-infiltrating immune cells in paired primary and RM NPC samples by targeted mRNA sequencing.

Results

We found that RM NPC, compared to their paired primary diseases, showed significant enrichment of immune cell-related signatures. This was associated with an altered immune cell composition, with enhanced T cell activation and exhaustion coupled with an M2-skewed macrophage population.

Conclusion

Together, these data depict a more inflamed yet immunosuppressive microenvironment of RM NPC and highlight macrophages being a potential target to reinvigorate antitumoural immune responses.

This abstract submission :

This is an encore abstract.

Category : Head and Neck Cancers (HNC)

ID : HNC 2

First Name : Kush Shah

Organisation : Manipal Hospitals

Title

EVALUATION OF POST-OPERATIVE FUNCTIONAL OUTCOMES IN OPERABLE TONGUE CANCERS.

Introduction

Tongue cancer is a common cancer in Indian subcontinent. Resection of tongue leads to functional deficits related to speech and swallowing. The appropriate method of tongue reconstruction is critical for better functional outcomes. Adjuvant Radiation also affects the long term functional outcomes significantly. The aim of this study was to determine the optimal reconstructive method for restoring postoperative function based on the extent of resection and the effect of adjuvant radiation on functional outcomes.

Methods

We prospectively observed 50 patients with operable anterior tongue cancer who underwent glossectomy within the hemi tongue between February 2019 to June 2020. Tongue mobility, articulation, speech intelligibility and swallowing outcomes were assessed at 1-,6- and 12 months post operatively and were analyzed according to extent of glossectomy, the method of reconstruction and the need of adjuvant treatment.

Results

Post-operative Speech intelligibility, tongue mobility and Swallowing scores were significantly better with Partial glossectomy than Hemi glossectomy(p<0.05 for all). Speech articulation scores were higher with partial glossectomy but did not reach statistical significance. In partial glossectomy cases, primary closure and secondary intention had better function in speech, tongue mobility and swallowing but only the swallowing function reached the statistical significance(p<0.001). In hemi glossectomy cases, the free flap reconstruction group had higher mean scores for tongue mobility, articulation and speech intelligibility than primary closure or secondary intention but they did not reach statistical significance. Swallowing score was no different among three methods of reconstruction in hemi glossectomy patients. Patients with Adjuvant RT had significantly worse functional outcomes than those who did not receive Adjuvant RT(p<0.05).

Conclusion

In conclusion, post-operative functions are inversely related with extent of tongue resection and oral tongue reconstruction should aim at restoring tongue mobility and bulk. For the smaller defects, primary closure or secondary intention is an acceptable method of reconstruction. Though larger resection of tongue preferably requires free flap reconstruction to improve post-operative functional outcomes. Adjuvant radiation therapy adversely affects long term functional outcomes after tongue cancer surgery.

This abstract submission :

This is an encore abstract.

Category : Immunotherapy (IMU)

ID : IMU 1

First Name : Mai Chan Lau

Organisation : A*STAR

Title

Spatially resolved multi-omics analysis for deciphering the radiotherapy-induced immunomodulation effect synergized with immunotherapy in hepatocellular carcinoma.

Introduction

Radiotherapy (RT) represents an important cancer treatment modality delivered to 50% of all cancer patients. Besides its direct effect of killing tumor cells, the secondary systemic effects of RT have been increasingly recognized. Through shaping the tumor microenvironment, RT can thus change responses to immunotherapy (IO), another major modality of cancer therapy due to the well-tolerated and durable antitumor activity. Multiple clinical trials have shown an overall improved response rate in HCC by combining RT with IO, however, treatment rates remain low and unpredictable. The suboptimal outcomes are largely due to a lack of knowledge of the underlying immunomodulation effect of RT and unavailability of an effective prognostic biomarker. On the other hand, using advanced spatial profiling assay like multiplexed immunofluorescence, our group and others have also demonstrated that cellular spatial organization within the tumor microenvironment plays a critical role in anti-tumor immunity. Hence, we sought to characterize the in-situ molecular immune responses and their spatial relationship with radiation source, for advancing our understanding of the systemic immunomodulation effect of RT and its synergistic benefits with IO.

Methods

Using digital spatial profiling (DSP), we profiled 1,800 transcripts in FFPE tissues collected from 4 responders and 8 non-responders treated with Y90-radioembolization and anti-PD-1 combination therapy. For each tissue collected post-RT, (i) four contiguous tissue regions at increasing distances to Y90 particle [for evaluating the spatial effect of RT on immune responses], and (ii) ROIs far from Y90 particle [for evaluating the systemic effects], were selected by a pathologist (JY). For each baseline tissue, multiple ROIs were also analyzed for assessing the overall RT effect by comparing with the post-RT data. All statistical analyses were performed in R; Tumor Immune Dysfunction and Exclusion (TIDE) analysis was performed using the web platform TIDE (http://tide.dfci.harvard.edu).

Results

Overall analysis of existing IO biomarkers, i.e., TIDE and immuno-predictive score (IMPRES), counter-intuitively indicated a decrease of IO-responsiveness in responders upon RT. Whereas, spatial investigation of underlying immune responses revealed that RT might have induced a systemic increasing of T cell exclusion and decreasing of T cell dysfunction in the non-responders but not in the responders. Moreover, a systemic increasing of the expression of CD274, the ligand of PD-1, was only seen in the responders. Gene deconvolution further revealed responders-specific enrichment of CD8 naïve T cells across all ROIs.

Conclusion

Our study suggested that existing IO biomarkers, i.e., TIDE and IMPRES, mainly tested in melanoma might not be directly applicable to HCC. Our spatial data revealed that enrichment of CD8 naïve T cells along with systemic increase of CD274 potentiated by RT in the responders might be the key immune determinants of anti-PD-1-mediated anti-tumor immunity. RT might have also caused T cell exclusion in the non-responders. Our on-going works include evaluation of immune cell-type specific systemic responses and exploration for novel biomarkers for predicting HCC patient response to RT-IO combination therapy.

Category : Immunotherapy (IMU)

ID : IMU 2

First Name : Jong-Mu Sun

Organisation : Samsung Medical Center, Sungkyunkwan University School of Medicine

Title

LEAP-014: An open-label, randomized, phase 3 study of first-line lenvatinib plus pembrolizumab plus chemotherapy in esophageal squamous cell carcinoma

Introduction

Recent data from the KEYNOTE-590 study demonstrated the superiority of pembrolizumab plus chemotherapy compared with chemotherapy as first-line treatment for unresectable locally advanced recurrent or metastatic adenocarcinoma or squamous cell carcinoma of the esophagus, or advanced/metastatic Siewert type 1 adenocarcinoma of the gastroesophageal junction. Prior data also suggest promising antitumor activity of lenvatinib plus pembrolizumab in advanced solid tumors. LEAP-014 (NCT04949256) is a randomized, 2-part, open-label, phase 3 study that will evaluate the efficacy and safety of first-line lenvatinib plus pembrolizumab plus chemotherapy versus pembrolizumab plus chemotherapy in patients with metastatic esophageal squamous cell carcinoma (ESCC).

Methods

Key eligibility criteria include metastatic ESCC, measurable disease per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1), and Eastern Cooperative Oncology Group performance status ≤1. In part 1 (safety run-in), ~6 patients will be treated for induction with intravenous (IV) pembrolizumab 400 mg every 6 weeks (Q6W) for 2 cycles plus oral lenvatinib 8 mg daily (QD) plus IV 5-fluorouracil (FU; 4000 mg/m^2 on days 1-5) plus IV cisplatin (80 mg/m^2) (FP) for 4 cycles and ~6 patients in China, Hong Kong, Republic of Korea, and Taiwan will be treated for induction with IV pembrolizumab 400 mg Q6W for 2 cycles plus oral lenvatinib 8 mg QD plus IV paclitaxel (175 mg/m^2) plus IV cisplatin (75 mg/m^2) (TP) for 4 cycles. All 12 patients will be treated for consolidation with pembrolizumab 400 mg Q6W for ≤16 doses plus lenvatinib 20 mg QD and closely monitored for 21 days after the first dose of study intervention for dose-limiting toxicities. In part 2 (main study), approximately 850 patients will be randomly assigned 1:1 to induction with pembrolizumab plus lenvatinib plus chemotherapy (FP or mFOLFOX6 [Q2W for 6 cycles {IV oxaliplatin 85 mg/m^2 plus bolus IV 5-FU 400 mg/m^2 plus continuous IV 5-FU 2400 mg/m^2 plus IV leucovorin 400 mg/m^2 or IV levoleucovorin 200 mg/m^2}] or TP [China, Hong Kong, Republic of Korea, and Taiwan only]) followed by consolidation with pembrolizumab plus lenvatinib (arm 1) or pembrolizumab plus chemotherapy (FP, mFOLFOX6, or TP [China, Hong Kong, Republic of Korea, and Taiwan only]; arm 2). Randomization will be stratified by PD-L1 combined positive score (CPS; ≥10 vs <10), region (East Asia vs North America and Western Europe vs rest of world), and chemotherapy backbone (FP vs TP vs mFOLFOX6). Treatment will continue until disease progression, unacceptable toxicity, or withdrawal of consent. Tumor imaging assessment will be performed Q6W for ≤1 year and Q9W thereafter. In part 1, the primary end point is safety and tolerability. In part 2, the dual primary end points are overall survival and progression-free survival (per RECIST v1.1 assessed by blinded independent central review [BICR]); secondary end points include objective response rate and duration of response (per RECIST v1.1 assessed by BICR) and safety and tolerability.

Results

Enrollment is ongoing.

Conclusion

Results of this study will provide clarity on the efficacy and safety of first-line lenvatinib plus pembrolizumab plus chemotherapy versus pembrolizumab plus chemotherapy in patients with metastatic ESCC.

This abstract submission :

This is an encore abstract.

Category : Immunotherapy (IMU)

ID : IMU 3

First Name : Jean-Philippe Metges

Organisation : CHU Brest, Institut de Cancerologie et d'Hematologie ARPEGO Network

Title

First-line Pembrolizumab Plus Chemotherapy Versus Chemotherapy in Advanced Esophageal Cancer: Longer-term Efficacy, Safety, and Quality-of-life Results From the Phase 3 KEYNOTE-590 Study

Introduction

In the phase 3 KEYNOTE-590 (NCT03189719) study, pembrolizumab plus chemotherapy compared with placebo plus chemotherapy (chemotherapy) showed superior OS, PFS, and ORR with a manageable adverse event (AE) profile in patients with untreated, advanced/unresectable or metastatic adenocarcinoma or esophageal squamous cell carcinoma (ESCC) or Siewert type 1 esophagogastric junction adenocarcinoma. Efficacy, safety, and health-related quality of life (HRQoL) after an additional 12 months of follow-up are reported.

Methods

Eligible patients were randomly assigned 1:1 to pembrolizumab 200 mg or placebo plus chemotherapy every 3 weeks for up to 35 cycles. Primary end points were OS in patients with ESCC PD-L1 combined positive score (CPS) ⩾10 tumors, and OS and PFS (RECIST v1.1 by investigator assessment) in patients with ESCC, PD-L1 CPS ⩾10, and all randomly assigned patients. Secondary end points included ORR, DOR, safety, and HRQoL. Data cutoff was July 9, 2021.

Results

Of 749 patients, 373 were randomly assigned to pembrolizumab plus chemotherapy and 376 to chemotherapy. Median follow-up, defined as time from randomization to data cutoff, was 34.8 months. OS was longer with pembrolizumab plus chemotherapy versus chemotherapy in patients with ESCC PD-L1 CPS ⩾10 (HR 0.59; 95% CI, 0.45-0.76), ESCC (0.73; 0.61-0.88), PD-L1 CPS ⩾ 10 (0.64; 0.51-0.80), and all randomly assigned patients (0.73; 0.63-0.86). In patients with adenocarcinoma, the OS HR was 0.73 (95% CI, 0.55-0.99). Estimated 24-month OS rate in all randomly assigned patients was 26.3% with pembrolizumab plus chemotherapy versus 16.1% with chemotherapy. PFS was longer with pembrolizumab plus chemotherapy versus chemotherapy in patients with ESCC (HR 0.65; 95% CI, 0.54-0.78), PD-L1 CPS ⩾10 (0.51; 0.41-0.65), and all randomly assigned patients (0.64; 0.55-0.75). Estimated 24-month PFS rate in all randomly assigned patients was 11.6% with pembrolizumab plus chemotherapy versus 3.3% with chemotherapy. Confirmed ORR was 45.0% (25 CR) with pembrolizumab plus chemotherapy versus 29.3% (9 CR) with chemotherapy. Median DOR was 8.3 months (range, 1.2+ to 41.7+) with pembrolizumab plus chemotherapy versus 6.0 months (1.5+ to 34.9+) with chemotherapy; 20.4% of patients in the pembrolizumab plus chemotherapy versus 6.2% of patients in the chemotherapy group had DOR ⩾24 months. Grade 3-5 treatment-related AE rates occurred in 71.9% of patients in the pembrolizumab plus chemotherapy group and 67.6% of patients in the chemotherapy group. There was no significant difference in least squares mean (LSM) change from baseline to week 18 between pembrolizumab plus chemotherapy versus chemotherapy in EORTC QLQ-C30 global health status/quality-of-life (LSM difference –0.10; 95% CI, –3.40 to 3.20). LSM change from baseline to week 18 was better with pembrolizumab plus chemotherapy versus chemotherapy for QLQ-OES 18 pain (–2.94; 95% CI, –5.86 to –0.02) and dysphagia (–5.54; 95% CI: –10.92 to –0.16).

Conclusion

With extended follow-up, pembrolizumab plus chemotherapy continued to maintain improvement in OS, PFS, and ORR versus chemotherapy and was associated with manageable AEs. HRQoL remained stable. These data reinforce previous observations from KEYNOTE-590 and support use of pembrolizumab plus chemotherapy as a new standard of care for patients with unresectable, metastatic esophageal cancer in the first-line setting.

This abstract submission :

This is an encore abstract.

Category : Lung Cancers and Other Intra-thoracic Malignancies (LUC)

ID : LUC 1

First Name : Chong Kin Liam

Organisation : University of Malaya

Title

Tepotinib + gefitinib in patients with EGFR-mutant NSCLC with MET amplification: Final analysis of INSIGHT

Introduction

In the INSIGHT trial primary analysis (NCT01982955; median follow-up: 21.8 months), tepotinib (a potent, highly selective, once-daily [QD] MET inhibitor) + gefitinib improved efficacy vs chemotherapy in patients with epidermal growth factor receptor (EGFR)-mutant non-small cell lung cancer (NSCLC) and resistance to EGFR tyrosine kinase inhibitor (TKI) therapy due to MET amplification (METamp) (Wu et al., Lancet Respir Med 2020). Here, we report final analyses from INSIGHT (data cut-off: Sept 3, 2021; median follow-up: 57.5 months).

Methods

Patients with EGFR-mutant (T790M-negative) NSCLC and anti-EGFR resistance, with MET gene copy number ⩾5 and/or MET:CEP7 ⩾2 by fluorescence in situ hybridization (METamp), and/or MET immunohistochemistry (IHC) 2+/3+ (MET overexpression), were randomized to tepotinib 500 mg (450 mg active moiety) + gefitinib 250 mg QD or chemotherapy. The primary endpoint was progression-free survival (PFS) per investigator assessment. Preplanned analyses evaluated patients with METamp.

Results

Of 55 randomized patients in the INSIGHT study, 19 (34.5%) had METamp (17 of whom were also MET IHC 3+). In patients with METamp, the median age was 60.4 years, 68.4% were never-smokers, and prior EGFR TKIs were gefitinib (57.9%), afatinib (21.1%), erlotinib (10.5%), and icotinib (10.5%). Median duration of tepotinib + gefitinib was 11.3 months (range: 1.1–56.5), with treatment duration >1 year in 6 patients (31.6%) and >4 years in 3 patients (15.8%). Two patients continued treatment outside the study. Tepotinib + gefitinib (n=12) improved outcomes vs chemotherapy (n=7). Respectively, median PFS was 16.6 vs 4.2 months (hazard ratio [HR]=0.13; 90% CI: 0.04, 0.43), median overall survival (OS) was 37.3 vs 13.1 months (HR=0.10; 90% CI: 0.02, 0.36), objective response rate was 66.7% vs 42.9% (odds ratio=2.67; 90% CI: 0.37, 19.56), and median duration of response was 19.9 (90% CI: 7.0, not estimable [ne]) vs 2.8 months (90% CI: 2.8, ne). Most common post-study therapies were kinase inhibitors (n=2 in the tepotinib + gefitinib arm; n=3 in the chemotherapy arm). Treatment-related Grade ⩾3 adverse events (AEs) occurred in 7 patients (58.3%) with tepotinib + gefitinib and 5 (71.4%) with chemotherapy. The most commonly reported treatment-related Grade ⩾3 AEs were amylase increased and lipase increased (both 33.3%) in the tepotinib + gefitinib arm, and anemia, neutrophil count decreased and white blood cell count decreased (all 28.6%) in the chemotherapy arm. In patients with MET IHC 3+ (n=34; including 17 patients with METamp), tepotinib + gefitinib also markedly improved PFS (HR=0.35; 90% CI: 0.17, 0.74) and OS (HR=0.44; 90% CI: 0.23, 0.84) vs chemotherapy.

Conclusion

Tepotinib + gefitinib greatly improved PFS and OS vs chemotherapy in patients with EGFR-mutant NSCLC with METamp. INSIGHT 2 is evaluating tepotinib + osimertinib in this setting.

This abstract submission :

This is an encore abstract.

Category : Lung Cancers and Other Intra-thoracic Malignancies (LUC)

ID : LUC 2

First Name : Terufumi Kato

Organisation : Kanagawa Cancer Center

Title

Tepotinib in Asian patients with advanced NSCLC with MET exon 14 skipping

Introduction

Tepotinib is a highly selective, potent MET inhibitor approved in several Asian countries for the treatment of advanced MET exon 14 (METex14) skipping non-small cell lung cancer (NSCLC). In the VISION study (n=275; data cut-off: Feb 1, 2021), tepotinib had an objective response rate (ORR) of 49.1% (95% CI: 43.0, 55.2) by independent review, with a median duration of response (mDOR) of 13.8 months (95% CI: 9.9, 19.4) across treatment lines. Here, we report outcomes in Asian patients.

Methods

Patients with advanced METex14 skipping NSCLC, detected by liquid (L+) or tissue (T+) biopsy, received tepotinib 500 mg (450 mg active moiety) once daily. The primary endpoint was objective response by independent review. Efficacy was assessed in 79 Asian patients with ⩾3 months' follow-up, and safety was assessed in 88 Asian patients who received tepotinib by data cut-off (Feb 1, 2021). Only patients enrolled in Asia were assessed for health-related quality of life (HRQoL).

Results

In 79 Asian patients assessed for efficacy (38% female, 42% smoking history, 34% treatment-naïve and 77% adenocarcinoma), ORR was 54.4% (95% CI: 42.8, 65.7), mDOR was 18.5 months (95% CI: 8.3, not estimable [ne]), median progression-free survival was 12.1 months (95% CI: 6.9, ne), and median overall survival was 20.4 months (95% CI: 19.1, ne). ORR was 66.7% (95% CI: 46.0, 83.5) in treatment-naïve patients (n=27) and 48.1% (95% CI: 34.0, 62.4) in previously treated patients (n=52). Meaningful activity was observed irrespective of the METex14 skipping detection method used; ORR in T+ patients (n=57) was 57.9% (95% CI: 44.1, 70.9) and, in L+ patients (n=37), ORR was 51.4% (95% CI: 34.4, 68.1). In treatment-naïve T+ patients (n=20), ORR was 70.0% (95% CI: 45.7, 88.1) and, in previously treated T+ patients (n=37), ORR was 51.4% (95% CI: 34.4, 68.1). In patients analyzed for HRQoL (n=73), mean change from baseline for EORTC QLQ-C30 GHS (4.06), EQ-5D-5L VAS (-0.53), and EORTC QLQ-LC13 symptom scores for cough (-6.77), dyspnea (-0.98), and chest pain (-7.00), demonstrated stability in QoL. In 88 Asian patients analyzed for safety, the most common adverse events (AEs) were peripheral edema, increased blood creatinine, and diarrhea. A total of 29.5% of patients had Grade ⩾3 treatment-related (TR) AEs. TRAEs led to dose reductions in 29.5%, temporary interruption in 43.2%, and permanent discontinuation in 14.8% of patients.

Conclusion

In VISION, tepotinib showed robust and durable clinical activity in Asian patients with METex14 skipping NSCLC. TRAEs were manageable, with few leading to treatment discontinuation. Overall, VISION enrolled 106 Asian patients with METex14 skipping NSCLC; analysis in this population is ongoing.

This abstract submission :

This is an encore abstract.

Category : Neuroendocrine Tumors (NET)

ID : NET 1

First Name : Juan Miguel Pena

Organisation : Asian Hospital and Medical Center

Title

DERMATOMYOSITIS ASSOCIATED WITH PULMONARY LARGE CELL NEUROENDOCRINE CARCINOMA: A CASE REPORT

Introduction

Dermatomyositis is a rare autoimmune inflammatory disease affecting the skin and muscles associated with an increased risk of solid tumors - affecting the ovaries, breast, colon and nasopharynx. There is a rare association between dermatomyositis and pulmonary large cell neuroendocrine carcinoma such that in a literature review of published material, only two cases have been reported internationally and none locally. Large cell neuroendocrine carcinoma (LCNEC) - in itself, is also a rare malignancy representing only 1-3% of all primary lung carcinomas.

Methods

Case Report

Results

This is a case of a 53-year-old filipina who presented with an eight-month history of facial erythema, swelling of bilateral metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints, and erythema over extensor surfaces of said joints. She had elevated creatine kinase MM and positive anti-nuclear antibody for which she was prescribed prednisone, to which she was uncompliant. She lost weight and experienced severe abdominal pain. Abdominal imaging revealed multiple confluent abdominal and thoracic lymphadenopathy with histopathology of LCNEC. Peculiarly, despite being a lung carcinoma, the scan showed no pulmonary masses or nodules. IHC stains of the lymph node were positive for neuroendocrine markers and negative for any mutation in the epidermal growth factor receptor. Her Ki-67, which is used as a prognostic factor and correlates with mitotic count - was 70% and PD-L1 tumor proportion score – a predictor of therapeutic effect - is 5-10%. She was diagnosed with dermatomyositis and pulmonary LCNEC and received 3 cycles of cisplatin and etoposide. After, she gained weight with resolution of musculocutaneous lesions. PET scan was repeated still showing multiple confluent paraaortic, aortocaval, pericaval lymph nodes with no significant interval change from the first PET scan. Pembrolizumab was started however, shortly, she expired due to Pneumonia. Conclusion: Among published data, we herein present the third reported case of dermatomyositis associated with pulmonary large cell neuroendocrine carcinoma worldwide and the first reported case in the Philippines thereby contributing to present medical literature. This demonstrates two rare diseases associated with each other and exemplifies the need for awareness of such disease entities. It demonstrates a rare case of LCNEC without any pulmonary masses or nodules. It also illustrates the importance of screening patients with dermatomyositis for malignancy and other immunocompromised states.

Conclusion

Among published data, we herein present the third reported case of dermatomyositis associated with pulmonary large cell neuroendocrine carcinoma worldwide and the first reported case in the Philippines thereby contributing to present medical literature. This demonstrates two rare diseases associated with each other and exemplifies the need for awareness of such disease entities. It demonstrates a rare case of LCNEC without any pulmonary masses or nodules. It also illustrates the importance of screening patients with dermatomyositis for malignancy and other immunocompromised states.

This abstract submission :

This is an encore abstract.

Category : Radiation Oncology (RAD)

ID : RAD 1

First Name : Chia Ching Lee

Organisation : National University Cancer Institute Singapore

Title

Stereotactic Body Radiation Therapy versus Conventional External Beam Radiation Therapy for Painful Bone Metastases: A Systematic Review and Meta-analysis of Randomized Trials

Introduction

The magnitude of benefit and toxicity of stereotactic body radiation therapy (SBRT) compared with conventional external beam radiation therapy (cEBRT) in treating symptomatic bone metastases is unclear due to the conflicting results from randomized controlled trials (RCTs). We performed a systematic review and meta-analysis to compare the efficacy and safety of SBRT and cEBRT in patients with previously unirradiated painful bone metastases.

Methods

We searched various databases and major oncologic conference proceedings from inception to Oct 2021 for RCTs comparing SBRT with cEBRT for previously unirradiated painful bone metastases. The outcomes of interest were efficacy (overall and complete pain response rates, local progression, overall survival (OS) and quality of life (QoL)) and safety (post-irradiation fractures, pain flares and radiation myelopathy). We assessed the methodologic quality of individual trials using the revised Cochrane risk-of-bias (RoB2) tool. We performed one-stage individual patient data meta-analysis using multilevel logistic regression model. Sensitivity analyses were conducted using two-stage frequentist and Bayesian meta-analyses. We adopted Synthesis Without Meta-analysis (SWiM) approach to summarize adverse events and quality of life outcomes. We assessed the certainty of the evidence for the efficacy outcomes using GRADE approach.

Results

Six RCTs including 894 patients were identified. Five of the included trials had low risk of bias. There was no significant difference in overall pain response rates at 3 months between SBRT and cEBRT (odd ratio (OR), 1.10; 95% confidence interval (CI), 0.84-1.44; P, 0.48; GRADE, moderate certainty). SBRT significantly improved complete pain response rates at 3 months (OR, 3.38; 95% CI, 1.88-6.07; 0.01; GRADE, high certainty) and reduced local progression rates (OR, 0.15; 95% CI, 0.04-0.53; 0.01; GRADE, high certainty), compared to cEBRT. Sensitivity analyses showed consistent findings. SBRT was associated with a modest increase in pain flare rates, compared to cEBRT. There were no significant differences between the two groups in OS, QoL, post-irradiation fracture and radiation myelopathy.

Conclusion

Among the patients with previously unirradiated symptomatic bone metastases, SBRT significantly improved complete but not overall pain response rates at 3 months and delayed local progression without adversely impacting on the quality of life and overall survival at the expense of a modestly increased risk of pain flare, compared to cEBRT.

This abstract submission :

This is an encore abstract.

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Title

Spatial transcriptomics-enabled machine learning approach for integrated morphology-transcriptome tumor cell phenotyping

Introduction

As part of the routine clinical workflow for cancer diagnosis, hematoxylin and eosin (H&E)-based pathologists' tumor subtyping based on tumor cell size, shape, and structure is used to inform treatment decisions. Meanwhile, transcriptomic analysis of various cancer types has revealed distinct tumor molecular subtypes associated with different tumorigenesis pathways, enabling molecularly informed treatments. Advancement in digital pathology and machine learning (ML) technologies has enabled the integration of histology and transcriptome, improving individualized treatment. However, current ML approaches have been limited to tissue-level characterization using bulk transcriptome, overlooking the importance of cell-level tumor heterogeneity. This limitation can be overcome by the recent development of spatial transcriptomics (ST) which enables in-situ transcriptomic profiling of tissues. Here, we aim to develop a ML morphology-transcriptomic approach to in-situ characterize tumor cells, through cell-level integration of H&E-staining and ST data.

Methods

ST of two tissue sections from a hepatocellular carcinoma (HCC) patient were profiled using 10× Visium platform. Using the companion H&E image, tissue regions were machine-learned as tumor epithelium and stroma, and individual cells were segmented (StarDist algorithm) with 53 H&E features (cellular morphologies and staining intensities) extracted, in QuPath (v0.3.2). The tumor epithelial cells (cells in the tumor epithelium) were unsupervisedly clustered using encoder-based ensemble method and a consensus score consisting of three clustering metrics was used to determine the optimal clustering solution (cluster numbers and feature encoding). The resulting tumor cell clusters were mapped to the ST, and non-negative factorization deconvolution was performed to determine the phenotypic gene signatures. Single sample gene set enrichment analysis was used for gene ontology (GO) analysis, using the hallmark gene sets in the molecular signatures database (MSigDB). All bioinformatic analysis was performed in Python (v3.8).

Results

Using 10 encoded features, four tumor cell clusters were detected in each HCC tissue, characterized by differential nuclear size of 30.32, 56.39, 92.25, and 147.03 □m2 in one tissue, and 41.25, 74.80, 112.07, and 165.86 □m2 in the other tissue, accounting for 43% (22,349), 34% (17,548), 18% (9,173), and 5% (2,782) tumor cells, and 35% (4,905), 34% (4,854), 25% (3,482) and 7% (956) tumor cells, respectively. Tumor cell subsets of similar nuclear sizes across the two tissues shared 55%-80% common pathways among the top 20. Tumor subsets with the smallest nuclei in both tissues were exclusively upregulated in inflammatory response pathway. In one of the tissues, spatial co-localization was observed between tumor cells with similar nuclear sizes (two smallest versus two largest).

Conclusion

Our ML approach revealed four morphologically distinct tumor cell subsets in each of the HCC tissues. These tumor subsets, even ones contributing <10% of total tumor cells, demonstrated high transcriptomic similarity across tissues. Our data thus demonstrated not only intra-patient tumor cell heterogeneity but also tumor phenotypes with spatial persistence across tissue sampling sites. On-going works include the investigation for differential immunogenicity through tumor- immune proximity analysis. Altogether, the morphology-transcriptome-defined tumor cell subsets would enable intricate dissection of underlying tumor biology, advancing individualized treatment.