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NEOPLASIA NEWS

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Dear Doctor,

The battle against Cancer is a collective effort. People all over the world stand united in their crusade. To assist everyone, we want to reach out to the world. With our innovations, we want to make good health a celebration,every-where. Already, we are making rapid strides on a level that's global. So, in any dialect, Spanish, Mexican, Italianor Hindi... Zuvius Lifesciences will always stand for **'Redefining health. Rediscovering life'.**

In redefining health, we will redefine customer satisfaction, also. We want you to know that we are there for you. For you, we'll try harder, we'll go that extra mile, never stopping, even for a moment, in our dedicated quest. Customer satisfaction that's par excellence is our motto - be it in our products, our services, our manufacturing facilities or in our ethos.

We understand that your time is precious and the data published on oncology is very vast.Through this issue we will be updating you with the latest and important updates in the field of oncology. Our medical team will always be there for you bringing together the cumulative expertise and experience, along with the inherent visionary zeal to keep on trying harder, to keep on innovating.

We look forward to your feedback and participation to make it more interactive. Feel free to send your Articles, feedback, queries & suggestions to our medical team at
neoplasianews@zuviuslifesciences.in

Regards

Nimish G. Thakkar

Chairman and Managing Director (CMD)

02

Long-term safety of growth hormone replacement therapy after childhood medulloblastoma and PNET: it is time to set aside old concerns.

J Neurooncol. 2016 Oct 21

Indini A, Schiavello E, Biassoni V, Bergamaschi L, Magni MC, Puma N, Chiaravalli S, Pallotti F, Seregni E, Diletto B, Pecori E, Gandola L, Poggi G, Massimino M.

To assess the long-term safety of administering growth hormone (GH) in patients with GH deficiency due to treatment for childhood medulloblastoma and primitive neuroectodermal tumor (PNET). Data were retrospectively retrieved on children receiving GH supplementation, assessing their disease-free and overall survival outcomes and risk of secondary malignancies using Kaplan-Meier and Cox models. Overall 65 children were consecutively collected from May 1981 to April 2013. All patients had undergone craniospinal irradiation (total dose 18-39 Gy), and subsequently received GH for a median (interquartile range, IQR) of 81 (50.6-114.9) months. At a median (IQR) of 122.4 months (74.4-149.5) after the end of their adjuvant cancer treatment, two patients (3%) experienced recurrent disease and 8 (12.3 %) developed secondary malignancies, all but one of them (an osteosarcoma) related to radiation exposure and occurring within the radiation fields. There was no apparent correlation between the administration of GH replacement therapy (or its duration) and primary tumor relapse or the onset of secondary malignancies [HR: 1.01 (95% CI: 0.98, 1.03) for every additional 12 months of GH supplementation; p=0.36). At univariate analysis, the large cell or anaplastic medulloblastoma subtype, metastases and myeloablative chemotherapy correlated with a higher risk of secondary malignancies ($p < 0.1$), but multivariate analysis failed to identify any factors independently associated with this risk. Our data supports once more the safety of long-term GH replacement therapy in children treated for medulloblastoma/PNET, previously reported in larger data sets. The neuro-oncology community now need to warrant large-scale meta-analyses or international prospective trials in order to consolidate our knowledge of factors other than GH, such as genetic predisposition, high-grade/metastatic disease, high-dose chemotherapy and era of treatment, in promoting the occurrence of secondary malignancies.

Characteristics and treatment of human epidermal growth factor receptor 2 positive breast cancer: 43,485 cases from the National Cancer Database treated in 2010 and 2011.

Am J Surg. 2016 Jul 21. pii: S0002-9610(16)30361-0. doi: 10.1016/j.amjsurg.2016.05.018

Killelea BK, Chagpar AB, Horowitz NR, Lannin DR

BACKGROUND:

Although identification of human epidermal growth factor receptor 2 (Her2) positive breast cancer represents one of the greatest advances over the past 3 decades, it has not been studied extensively on a national level.

METHODS:

The National Cancer Database is a joint project of the American Cancer Society and the American College of Surgeons and contains data on about 70% of the cancer cases in the United States. Data on Her2 have been collected since 2010 and was used for this study.

RESULTS:

Of 298,937 cases of invasive breast cancer with known Her2 status diagnosed in 2010 and 2011, 43,485 (14.5%) were Her2 positive. Her2 positivity was greatest in Asian/Pacific Islanders and least in non-Hispanic Whites and was markedly more common in younger women. The incidence of Her2 positive tumors ranged from a low of 13.9% in the Mountain West region to a high of 16.0% in the West South Central region (P < .001). Compared with Her2 negative tumors, Her2 positive tumors were larger (2.6 vs 2.2 cm, P < .001), more likely to have positive nodes (39% vs 31% P < .001), have lymphovascular invasion (30% vs 20%, P < .001), and be high grade (56% vs 29%, P < .001). There were also differences by histology: invasive ductal 16.4%, invasive lobular 5.5%, tubular 2.3%, inflammatory 36%, and Paget's with invasion 59%. When adjusted for age, race, tumor size, and nodal status Her2 positive tumors were much more likely to receive chemotherapy (odds ratio = 5.5, confidence interval = 5.2 to 6.0) and somewhat less likely to undergo breast preservation (odds ratio = .78, confidence interval = .76 to .80).

CONCLUSIONS:

Her2 positive tumors have distinct epidemiologic, clinical, and treatment characteristics.

04

Comparison of gemcitabine plus cisplatin versus capecitabine plus cisplatin as first-line chemotherapy for advanced biliary tract cancer

Asia Pac J Clin Oncol. 2016 Oct 22. doi: 10.1111/ajco.12592.

Park K, Kim KP, Park S, Chang HM

AIM:
It remains unclear whether capecitabine combined with cisplatin would show similar effects compared with standard therapy using gemcitabine and cisplatin in advanced biliary tract cancer (BTC).
METHODS:
Patients with advanced BTC who were treated with first-line chemotherapy at Asan Medical Center were retrospectively analyzed. All patients received either cisplatin followed by gemcitabine on days 1 and 8 every 3 weeks (GP group), or capecitabine on days 1-14 with cisplatin on day 1 every 3 weeks (XP group).
RESULTS:
Of the 134 patients who met the inclusion criteria, 78 received XP and 56 were treated with GP. After a median follow-up of 26.2 months, the progression-free survival was 5.7 months for XP versus 4.1 months for GP (hazard ratio [HR] = 0.81, P = 0.31). The overall survival (OS) was 11.0 months for XP versus 9.8 months for GP (HR = 0.84, P = 0.36). In the multivariate analysis, there were no significant differences in PFS and OS between the two groups.
CONCLUSION:
XP seems to be as effective as GP in patients with advanced BTC. The XP regimen is feasible and might offer increased convenience regarding the schedule of drug administration.

05

Can chemotherapy boost the survival benefit of adjuvant radiotherapy in early stage cervical cancer with intermediate risk factors? A population based study

Gynecol Oncol. 2016 Oct 18. pii: S0090-8258(16)31499-8. doi: 10.1016/j.ygyno.2016.10.022

Mahmoud O, Hathout L, Shaaban SG, Elshaikh MA, Beriwal S, Small W Jr

PURPOSE:

The Gynecologic Oncology group (GOG) 0263 trial is currently exploring whether adding chemotherapy to adjuvant radiotherapy improves recurrence-free and/or overall survival in stage IB-IIA cervical cancer patients with pathologic intermediate-risk factors. Using the National Cancer Data Base, we evaluated the benefit of adjuvant chemoradiotherapy over adjuvant radiotherapy alone in the community practice setting.

MATERIALS:

The analysis included 869 stage IB-IIA cervical cancer patients who underwent radical hysterectomy retrieving intermediate-risk factors justifying adjuvant therapy. Adjuvant chemoradiotherapy and adjuvant radiotherapy were delivered in 440 and 429 patients, respectively. Chi-square test assessed the distribution of variables in each group and the overall survival was estimated using the Kaplan-Meier method. Proportional hazard models were performed to evaluate the impact of the different prognostic factors on survival and propensity score analysis adjusted variables imbalanced distribution.

RESULTS:

Adding chemotherapy to ART did not show a survival benefit at 48months median follow-up; the 5-year overall survival was 87% and 81% (p=0.6) in the adjuvant chemoradiotherapy and adjuvant radiotherapy groups, respectively. On univariate analysis, age older than 60, a higher comorbidity score, and stage IIA were significantly associated with worse survival, while none of the other covariates were significant prognosticator on multivariate analysis. The same findings held after propensity score analysis.

CONCLUSION:

Our analysis could not detect a significant survival benefit for adjuvant chemoradiotherapy over adjuvant radiotherapy in women with intermediate-risk factors. Until GOG 0263 results become available, the benefits of adjuvant chemoradiotherapy should be considered on an individual basis within a multidisciplinary approach.

06

Prognostic Factor Analysis in Patients With Small-Cell Lung Cancer Treated With Third-Line Chemotherapy

Clin Lung Cancer. 2016 Nov;17(6):581-587. doi: 10.1016/j.cllc.2016.05.022.
Saruwatari K, Umemura S, Nomura S, Kirita K, Matsumoto S, Yoh K, Niho S, Ohmatsu H, Ohe Y, Goto K

BACKGROUND:
There is little information on the clinical outcome of patients with small-cell lung cancer (SCLC) treated with third-line chemotherapy. The purpose of this study was to clarify the prognostic factors of SCLC patients receiving third-line chemotherapy.
PATIENTS AND METHODS:
Between November 2001 and October 2011, 202 of 648 consecutive SCLC patients at the National Cancer Center Hospital East received third-line chemotherapy. Multivariate Cox regression analysis was performed to identify the prognostic factors for overall survival after third-line chemotherapy.
RESULTS:
The demographics of the 202 patients were as follows: median age 66 years, 83% male, and Eastern Cooperative Oncology Group (ECOG) performance status (PS) 0, 1, 2, and 3 values of 22, 122, 49, and 9, respectively. Median time to treatment failure after second-line chemotherapy (TTF2) was 4.5 months (TTF2 ≥ 5/< 5 months, 82/120). The median overall survival after third-line chemotherapy was 5.1 months. Multivariate Cox regression analysis showed that PS 0-1 (hazard ratio, 0.38; 95% confidence interval, 0.27-0.54; P < .001) and TTF2 ≥ 5 months (hazard ratio, 0.57; 95% confidence interval, 0.41-0.79; P < .001) were independent prognostic factors. TTF2 threshold of 5 months was determined on the basis of concordance probability adjusted by PS.
CONCLUSION:
PS 0-1 and TTF2 ≥ 5 months were associated with a favorable prognosis among SCLC patients receiving third-line chemotherapy. These 2 factors might be helpful for the selection of candidates for third-line chemotherapy and for patient stratification when conducting future clinical trials in the third-line setting.

07

Optimizing Survival of Patients With Marginally Operable Stage IIIA Non-Small-Cell Lung Cancer Receiving Chemoradiotherapy With or Without Surgery

Clin Lung Cancer. 2016 Nov;17(6):550-557. doi: 10.1016/j.cllc.2016.05.013

Yang KL, Chang YC, Ko HI, Chi MS, Wang HE, Hsu PS, Lin CC, Yeh DY, Kao SJ, Jiang JS, Chi KH

BACKGROUND:

For marginally operable stage IIIA non-small-cell lung cancer (NSCLC), surgery might not be done as planned after neoadjuvant concurrent chemoradiotherapy (CCRT) for reasons (unresectable or medically inoperable conditions, or patient refusal). This study aims to investigate the outcomes of a phased CCRT protocol established to maximize the operability of marginally operable stage IIIA NSCLC and to care for reassessed inoperable patients, in comparison with continuous-course definitive CCRT.

MATERIALS AND METHODS:

Forty-seven patients with marginally operable stage IIIA NSCLC receiving CCRT were included. Twenty-eight patients were treated with our phased CCRT protocol, including neoadjuvant CCRT followed by surgery (group A, n = 16) or, for reassessed inoperable patients, maintenance chemotherapy and split-course CCRT boost (group B, n = 12). The other 19 were treated with continuous-course definitive CCRT (group C). Overall survival (OS) and progression-free survival (PFS) were analyzed.

RESULTS:

Among all, median OS and PFS were 35.6 and 12.8 months, respectively (median follow-up, 22.3 months). The median OS of group A (not reached) was better than that of group B (34.4 months) and group C (15.2 months) (P = .009). On multivariate analysis, performance status 0 to 1 (hazard ratio [HR], 0.026; P < .001), adenocarcinoma (HR, 0.156; P = .003), and group A (HR, 0.199; P = .033) were independent prognostic factors. The OS of group B (HR, 0.450; 95% confidence interval, 0.118-1.717; P = .243) was not statistically different from that of group C.

CONCLUSIONS:

For marginally operable stage IIIA NSCLC, our phased CCRT strategy may optimize survival by maximizing operability and maintain an acceptable survival for reassessed inoperable patients by split-course CCRT boost following maintenance chemotherapy.

08

A childhood chemotherapy protocol improves overall survival among adults with T-lymphoblastic lymphoma.

Oncotarget. 2016 Jun 21;7(25):38884-38891. doi: 10.18632/oncotarget.9144.
Zhu MY, Wang H, Huang CY, Xia ZJ, Chen XQ, Geng QR, Wang WD, Wang L, Lu Y

A broadly accepted standard treatment for adult T-lymphoblastic lymphoma (T-LBL) has not yet been defined. To address that issue, we retrospectively compared three chemotherapy regimens used to treat 110 adult patients with newly diagnosed T-LBL. These included two adult regimens (ECOG2993 and hyper-CVAD) and a childhood regimen (BFM-90). These intensive drug regimens are mainly used to treat childhood and adult acute lymphoblastic leukemia. They included induction, consolidation, and maintenance chemotherapy protocols and were administered over the course of 2 years. Seventy-five patients (80%) achieved a complete remission (CR). Within a median follow-up time of 31 months (range: 5-152 months), the 5-year overall survival (OS) and progression-free survival (PFS) rates were 47.7% (95% CI, 35.0-69.8%) and 45.7% (95% CI, 27.6-56.6%), respectively. Shorter survival was associated with age > 40 years, poor ECOG PS and bone marrow involvement. Elevated lactic dehydrogenase (LDH) level, Ann Arbor stage and International Prognostic Index (IPI) score had no prognostic value. The childhood chemotherapy regimen improved CR and the overall survival rate more than the adult regimen in patients aged < 40 years.

09

Survival differences between patients with Hodgkin lymphoma treated inside and outside clinical trials. A study based on the EORTC-Netherlands Cancer Registry linked data with 20 years of follow-up

Br J Haematol. 2016 Oct 21. doi: 10.1111/bjh.14379
Liu L, Giusti F, Schaapveld M, Aleman B, Lugtenburg P, Meijnders P, Hutchings M, Lemmens V, Bogaerts J, Visser O

The survival of patients diagnosed with Hodgkin lymphoma (HL) has improved from 70% to 90% in clinical trials. However, population-based data has shown lower survival. In this study, clinical trial data were linked with cancer registry to identify trial and non-trial participants and differences in overall survival and associated factors were assessed. In 1986-2004, 27% of HL patients aged 15-70 years participated in clinical trials. Compared to non-trial participants, trial participants were younger (median age, 31 vs. 34 years), had staging registered more accurately and had an 8% higher 20-year survival rate (73% vs. 65%). After adjusting for baseline differences, no differences in survival (hazard ratio = 0·96, 95% confidence interval 0·82-1·12), or in subgroup analysis according to stage, remained. Over time, increased administration of chemotherapy in combination with radiotherapy, together with the decreased use of radiotherapy alone was observed among the trial population. This trend was later followed in non-trial participants, coinciding with a similar 'take-up' in survival. The observed superior survival among patients with HL treated in clinical trials can be largely explained by the differences in baseline characteristics, particularly younger age. High trial participation rate and centralized expertise facilitates the implementation of trial findings to real-world practice.

10

Whole body magnetic resonance imaging in newly diagnosed multiple myeloma: early changes in lesional signal fat fraction predict disease response

Br J Haematol. 2016 Oct 21. doi: 10.1111/bjh.14401.

Liu L, Giusti F, Schaapveld M, Aleman B, Lugtenburg P, Meijnders P, Hutchings M, Lemmens V, Bogaerts J, Visser O

Cross-sectional imaging techniques are being increasingly used for disease evaluation in patients with multiple myeloma. Whole body magnetic resonance imaging (WB-MRI) scanning is superior to plain radiography in baseline assessment of patients but changes following treatment have not been systematically explored. We carried out paired WB-MRI scans in 21 newly diagnosed patients prior to, and 8-weeks after, starting chemotherapy, and analysed stringently selected focal lesions (FLs) for parametric changes. A total of 323 FLs were evaluated, median 20 per patient. At 8 weeks, there was a reduction in estimated tumour volume (eTV), and an increase in signal fat fraction (sFF) and apparent diffusion coefficient (ADC) in the group as a whole (P < 0·001). Patients who achieved complete/very good partial response (CR/VGPR) to induction had a significantly greater increase in sFF compared to those achieving ≤ partial response (PR; P = 0·001). When analysed on a per-patient basis, all patients achieving CR/VGPR had a significant sFF increase in their FL's, in contrast to patients achieving ≤PR. sFF changes in patients reaching maximal response within 100 days (fast responders) were greater compared to slow responders (P = 0·001). Receiver Operator Characteristic analysis indicated that sFF changes at 8 weeks were the best biomarker (area under the Curve 0·95) for an inferior response (≤PR). We conclude that early lesional sFF changes may provide important information on depth of response, and are worthy of further prospective study.

11

Outcome of primary cutaneous anaplastic large cell lymphoma: a 20-year British Columbia Cancer Agency experience

Br J Haematol. 2016 Oct 21. doi: 10.1111/bjh.14404

Hapgood G, Pickles T, Sehn LH, Villa D, Klasa R, Scott DW, Gerrie AS, Gascoyne RD, Slack GW, Parsons C, Morris JW, Connors JM, Savage KJ

Primary cutaneous anaplastic large cell lymphoma (PCALCL) is a rare CD30+ lymphoproliferative disorder with excellent outcomes reported despite frequent cutaneous relapses. Limited information exists on the development of systemic lymphoma. The British Columbia Cancer Agency (BCCA) Lymphoid Cancer Database was searched to identify all adults diagnosed with PCALCL from 1993 to 2013. From 2005, the BCCA endorsed radiotherapy (RT) alone for limited stage with data failing to support chemotherapy. Forty-seven patients were identified with a male predominance (n = 31, 66%), median age of 64 years and predominantly limited stage (n = 40, 85%). Median follow-up was 8·4 years. The 5-year time to progression (TTP) was 58% (64% limited versus 29% advanced stage). The 5-year disease-specific survival (DSS) and overall survival was 86% and 75%, respectively. In an as-treated analysis, the 5-year DSS for limited stage patients was similar comparing RT to combined modality treatment or chemotherapy alone but the 5-year TTP favoured RT (82% vs. 33%, P = 0·004). The 5-year cumulative risk of developing systemic lymphoma was 14%. Our results confirm the favourable prognosis of PCALCL despite a high relapse rate. Limited stage patients treated with RT alone have excellent outcomes. There is a small risk of systemic lymphoma in PCALCL.

12

Brain structure and function in patients with ovarian cancer treated with first-line chemotherapy: a pilot study

Brain Imaging Behav. 2016 Oct 20

Correa DD, Root JC, Kryza-Lacombe M, Mehta M, Karimi S, Hensley ML, Relkin N

Women with ovarian cancer often undergo chemotherapy involving multiple agents. However, little is known about treatment-related central neurotoxicity in this population. The goal of this cross-sectional study was to assess brain structure and function and neurocognitive abilities in patients with ovarian cancer following first-line chemotherapy. Eighteen patients with ovarian, peritoneal and fallopian tube cancer and eighteen healthy controls matched for gender, age and education participated in the study. The patients were evaluated 1-4 months following completion of first-line taxane/platinum chemotherapy. All participants underwent structural and functional magnetic resonance imaging (MRI), and completed neuropsychological tests of attention, memory and executive functions. Neuroimaging assessments included voxel-based morphometry (VBM) for measuring gray matter (GM) volume, and functional MRI (fMRI) during the N-back working memory task. The results of VBM showed that patients had significantly reduced GM volume compared to healthy controls in the right middle/superior frontal gyrus, and in the left supramarginal gyrus and left inferior parietal lobule. fMRI results indicated significantly decreased activation in patients relative to healthy controls in the left middle frontal gyrus and left inferior parietal lobule during the N-back task (1/2/3-back >0-back). There were no statistically significant differences between the two groups on the neuropsychological tests. This is the first study showing structural and functional alterations involving frontal and parietal regions in patients with ovarian cancer treated with first-line chemotherapy. These findings are congruent with studies involving women with breast cancer, and provide additional supporting evidence for central neurotoxicity associated with taxane/platinum chemotherapy.

13

Temozolomide low-dose chemotherapy in newly diagnosed low-grade gliomas: activity, safety, and long-term follow-up

Tumori. 2016 Sep 22:0. doi: 10.5301/tj.5000565

Villani V, Merola R, Vidiri A, Fabi A, Carosi M, Giannarelli D, Marucci L, Maschio M, Carapella CM, Pace A

PURPOSE:

To explore the efficacy and toxicity of an extended schedule of temozolomide (50 mg/mq 1 week on/1 week off) in a population of newly diagnosed low-grade gliomas (LGG).

METHODS:

Primary endpoints were progression-free survival (PFS) at 12 and 24 months and response rate evaluated with Response Assessment in Neuro-Oncology Criteria. Secondary endpoints were clinical benefit (reduction of seizures frequency), reduction of steroid, and modifications of Karnofsky Performance Status.

RESULTS:

From 2006 to 2009, we enrolled 14 consecutive patients with newly diagnosed LGG: 8 grade II astrocytomas, 2 oligodendroglioma, and 4 oligo-astrocytoma. Temozolomide was administered for 18 cycles (mean) per patient (range 3-24 cycles). In 57.5% (n = 8), we observed stable disease, 28.5% (n = 4) presented a minor response, and 14% (n = 2) showed progression. Five patients presented early progression during the first year of treatment and the study was stopped. A relevant clinical benefit was observed in 85% of patients (seizure control). After 6 years of follow-up, only 4 patients died. Prolonged PFS was associated with 1p-19q codeletion over 1p-19q intact (35 vs 4 months; p<0.04) and IDH1 mutation over IDH1 wild-type (36 vs 6 months; p<0.009).

CONCLUSIONS:

The study was interrupted for the high rate of progression observed in the first 14 patients enrolled. However, our results show that an extended low dose of temozolomide presents interesting activity with objective response and clinical benefit, but does not seem to prevent progression in patients presenting unfavorable molecular prognostic factors.

14

Safety and efficacy of dose-dense chemotherapy with TCF regimen in elderly patients with locally advanced or metastatic gastric cancer

Tumori. 2016 Aug 23:0. doi: 10.5301/tj.5000556

Liguigli W, Tomasello G, Toppo L, Poli R, Lazzarelli S, Negri F, Perrucci B, Curti A, Brighenti M, Donati G, Nazzari M, Martinotti M, Vismarra M, Rovatti M, Passalacqua R

PURPOSE:
To evaluate the efficacy and safety of dose-dense TCF in elderly (≥65 years) compared to younger patients.
METHODS:
Safety and efficacy data relative to 119 consecutive patients with locally advanced or metastatic gastric cancer treated at our institution and enrolled in different phase II trials were retrospectively collected. All patients were treatment-naive and received docetaxel 70 mg/m2 day 1, cisplatin 60 mg/m2 day 1, l-folinic acid 100 mg/m2 days 1-2, followed by 5-fluorouracil 400 mg/m2 bolus days 1-2, and then 600 mg/m2 as a 22-hour continuous infusion days 1-2, every 14 days, plus pegfilgrastim 6 mg on day 3. Sixty patients (50%) aged ≥65 years received the same schedule with a dose reduction by 30%.
RESULTS:
A total of 86% of patients were evaluable for response and all for toxicity. In patients aged ≥65 years, we observed an overall response rate of 51%. Median overall survival was 11.2 (95% confidence interval [CI] 7.3-15.1) and 11.8 months (95% CI 9.2-16.2) in elderly and younger patients, respectively. In the elderly patients, the most frequent grade 3-4 toxicities were neutropenia (13%), leukopenia (7%), thrombocytopenia (18%), anemia (3%), and febrile neutropenia (8%); in the younger patients, neutropenia (56%), leucopenia (31%), thrombocytopenia (22%), anemia (15%), and febrile neutropenia (15%).
CONCLUSIONS:
Elderly patients can be safely treated with a dose-dense TCF regimen with a 30% dose reduction achieving similar efficacy results as younger patients with lesser toxicity.

15

Preoperative FOLFIRINOX for borderline resectable pancreatic cancer: Is radiation necessary in the modern era of chemotherapy?

J Surg Oncol. 2016 Oct;114(5):587-596. doi: 10.1002/jso.24375

Kim SS, Nakakura EK, Wang J, Kim GE, Corvera CU, Harris HW, Kirkwood KS, Hirose R, Tempero MA, Ko AH

BACKGROUND:

No consensus exists regarding the optimal neoadjuvant treatment paradigm for patients with borderline resectable pancreatic cancer (BRPC), including the respective roles of chemotherapy and radiation.

METHODS:

We performed a retrospective analysis, including detailed pathologic and radiologic review, of pancreatic cancer patients undergoing FOLFIRINOX, with or without radiation therapy (RT), prior to surgical resection at a high-volume academic center over a 4-year period.

RESULTS:

Of 26 patients meeting inclusion criteria, 22 (84.6%) received FOLFIRINOX alone without RT (median number of treatment cycles = 9). The majority of patients met formal radiographic criteria for BRPC, with the superior mesenteric vein representing the most common vessel involved. R0 resection rate was 90.9%, with 12 patients (54.5%) requiring vascular reconstruction. Treatment response was classified as moderate or marked in 16 patients (72.7%) according to the College of American Pathologists grading system. Estimated median disease-free and overall survival rates are 22.6 months and not reached (NR), respectively.

CONCLUSIONS:

This is one of the largest series to describe the use of neoadjuvant FOLFIRINOX, without radiation therapy, in patients with BRPC undergoing surgical resection. Given the high R0 resection rates and favorable clinical outcomes with chemotherapy alone, this strategy should be further assessed in prospective study design.

16

Feasibility and benefit of concurrent chemoradiotherapy for elderly patients with uterine cervical cancer

Tumori. 2016 Jul 19:0. doi: 10.5301/tj.5000530

Nosaka K, Shibata K, Utsumi F, Yoshida K, Niimi K, Sekiya R, Suzuki S, Kajiyama H, Kikkawa F

BACKGROUND:

Elderly patients with uterine cervical cancer reportedly have a poorer prognosis than younger patients. Until now, the benefit of concurrent chemoradiotherapy (CCRT) for elderly patients has been considered limited.

METHODS:

We retrospectively analyzed 49 women with cervical cancer aged >70 years primarily treated with radiotherapy (RT) or CCRT in our institute between 2003 and 2014. Treatment compliance, toxicity, and survival benefit were analyzed.

RESULTS:

A total of 49 patients were identified in this retrospective analysis. Twenty patients with a median age of 75.4 years (range 70-77) were treated with CCRT and 29 patients with a median age of 77.9 years (range 70-89) underwent RT. In the CCRT group, 14 patients (70%) completed CCRT consisting of radiotherapy and 5 courses of cisplatin plus 5-fluorouracil including patients requiring a dose reduction of chemotherapy. The median overall survival (OS) in the CCRT and RT groups was 66.9 and 60.1 months, respectively (p = 0.156). The most common grade 3/4 acute toxicity was hyponatremia (35.0%), followed by neutropenia (15.0%) and diarrhea (10.0%) in the CCRT group, while this was anemia (17.2%) followed by radiation enteritis (10.3%) in the RT group.

CONCLUSIONS:

CCRT was well tolerated in elderly patients with cervical cancer. Careful attention should be paid to the different characteristics of treatment-related toxicities in this group compared with younger patients.

17

Neutrophil-lymphocyte ratio as a prognostic marker for chemotherapy in advanced lung cancer

Int J Biol Markers. 2016 Jul 12:0. doi: 10.5301/jbm.5000222.
Liu ZL, Zeng TT, Zhou XJ, Ren YN, Zhang L, Zhang XX, Ding ZY

BACKGROUND:
Lung cancer ranks first both in morbidity and mortality in malignancies, but prognostic biological markers are lacking. The neutrophil-lymphocyte ratio (NLR) was proposed as a convenient biological marker. This study aimed to explore the prognostic value of NLR in advanced non-small cell lung cancer (NSCLC).
METHODS:
This retrospective study screened patients admitted from October 2007 to October 2014. Patients had histopathologically confirmed, treatment-naïve, metastatic NSCLC, and were prescribed platinum doublet chemotherapy. NLR and demographic data were collected, together with the outcome of chemotherapy. Progression-free survival (PFS) and overall survival (OS) were analyzed using the Kaplan-Meier method and Cox regression model.
RESULTS:
A total of 325 patients were enrolled. The cutoff value for NLR (3.19) was determined by receiver operator characteristic analysis. Patients were dichotomized into high (≥3.19) and low (<3.19) NLR groups. Both groups had similar demographic features. However, the low-NLR group had longer PFS (6.1 months) and OS (22.3 months) than the high-NLR group (5.1 months, p = 0.002; 13.1 months, p<0.001, respectively). Multivariate analysis confirmed that NLR was inversely related to the prognosis of these patients (HR = 1.684, 95%: 1.297-2.185, p<0.001).
CONCLUSIONS:
This study argues that NLR is a convenient prognostic biological marker for advanced NSCLC patients treated with first-line chemotherapy and warrants further validation.

18

Rectal cancers with microscopic circumferential resection margin involvement (R1 resections): Survivals, patterns of recurrence, and prognostic factors

J Surg Oncol. 2016 Oct;114(5):642-648. doi: 10.1002/jso.24360

Gravante G, Hemingway D, Stephenson JA, Sharpe D, Osman A, Haines M, Pirjamali V, Sorge R, YeungJM, Norwood M, Miller A, Boyle K

BACKGROUND AND OBJECTIVES:

We have reviewed our series of rectal cancer patients with circumferential resection margin involvement (R1) with particular regard to survival and prognostic factors.

METHODS:

R1 rectal cancer patients undergoing surgery at the Leicester Royal Infirmary between 1998 and 2008. Age, gender, radiological, and pathological tumor characteristics, neoadjuvant and adjuvant therapies were examined as prognostic factors on the overall survival (OS) and disease-free survival (DFS) at 5-year follow-up.

RESULTS:

A total of 885 rectal cancers were reviewed. Six hundred ninety-nine patients underwent a mesorectal excision and 71 of them were R1 resections (12.9%). OS was 43.7% (CI95% 33.5-53.8%; median survival 39 months). DFS was 57.4% (CI95% 43.0-71.8%; median survival 31 months). Pelvic recurrence rate occurred in 16 patients (26.2%, CI95% 16.5-36.0%), systemic recurrence rate in 23 patients (37.7%, CI95% 25.5-49.9%). At Cox-regression LNR and adjuvant chemotherapy were associated with both OS and DFS. No significant association was found between OS or DFS and adjuvant radiotherapy.

CONCLUSIONS:

In our series of R1 patients, the rates of local recurrence and OS at 5 years were 26.2% and 43.7%, respectively. Factors influencing systemic recurrences (LNR, adjuvant chemotherapy) are more associated with OS and DFS than those potentially affecting locoregional recurrences (adjuvant radiotherapy).

19

Is ovarian cancer a targetable disease? A systematic review and meta-analysis and genomic data investigation

Oncotarget. 2016 Oct 13. doi: 10.18632/oncotarget.12633.
Staropoli N, Ciliberto D, Chiellino S, Caglioti F, Giudice TD, Gualtieri S, Salvino A, Strangio A, Botta C, Pignata S, Tassone P, Tagliaferri P

OBJECTIVES:
The current gold-standard for the first-line treatment in IIIb/IV stages of epithelial ovarian cancer (EOC) is the combination of carboplatin and paclitaxel plus bevacizumab in some countries. In the era of personalized medicine, there is still uncertainty on the impact of several molecularly targeted agents, which have been investigated for the management of this disease. To shed light on the actual role of targeted therapy in EOC, a systematic review and meta-analysis was performed.
METHODS:
Clinical trials were selected by searching "Pubmed" database and abstracts from major cancer meetings within the time-frame of January 2004-June 2015. The endpoints were survival outcome and response rate (RR). Hazard ratios (HRs) of survival outcomes, with confidence intervals and odds-ratios (ORs) of RR, were extracted from retrieved studies and used for current analysis. Meta-analysis was carried out by random effect model.
RESULTS:
30 randomized trials for a total of 10,530 patients were selected and included in the final analysis. A benefit in terms of OS (pooled HR 0.915; 95%CI 0.840-0.997; p=0.043), particularly for anti-angiogenetic agents (HR 0.872; 95%CI 0.761-1.000; p=0.049), has been demonstrated for targeted therapy. Moreover, a significant advantage in platinum-resistant subgroup in term of PFS (HR 0.755; 95%CI 0.624-0.912; p=0.004) was found.
CONCLUSIONS:
This systematic review and meta-analysis provide the first evidence that targeted therapy is potentially able to translate into improved survival of EOC patients, with a major role played by anti-angiogenetic drugs. The role of target therapy is underlined in the platinum-resistant setting that represents the "pain in the neck" in EOC management.

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Tumor-infiltrating Neutrophils is Prognostic and Predictive For Postoperative Adjuvant Chemotherapy Benefit in Patients With Gastric Cancer

Ann Surg. 2016 Oct 14. [Epub ahead of print]

Zhang H, Liu H, Shen Z, Lin C, Wang X, Qin J, Qin X, Xu J, Sun Y

OBJECTIVE:

This study was aimed to investigate the prognostic value of tumor-infiltrating neutrophils (TINs) and to generate a predictive model to refine postoperative risk stratification system for patients with gastric cancer.

BACKGROUND:

TIN presents in various malignant tumors, but its clinical significance in gastric cancer remains obscure.

METHODS:

The study enrolled 3 independent sets of patients with gastric cancer from 2 institutional medical centers of China. TIN was estimated by immunohistochemical staining of CD66b, and its relationship with clinicopathological features and clinical outcomes were evaluated. Prognostic accuracies were evaluated by C-index and Akaike information criterion.

RESULTS:

TINs in gastric cancer tissues ranged from 0 to 192cells/high magnification filed (HPF), 0 to 117cells/HPF, and 0 to 142cells/HPF in the training, testing, and validation sets, respectively. TINs were negatively correlated with lymph node classification (P = 0.007, P = 0.041, and P = 0.032, respectively) and tumor stage (P = 0.019, P = 0.013, and P = 0.025, respectively) in the 3 sets. Moreover, multivariate analysis identified TINs and tumor node metastasis (TNM) stage as 2 independent prognostic factors for overall survival. Incorporation of TINs into well-established TNM system generated a predictive model that shows better predictive accuracy for overall survival. More importantly, patients with higher TINs were prone to overall survival benefit from postoperative adjuvant chemotherapy. These results were validated in the independent testing and validation sets.

CONCLUSIONS:

TIN in gastric cancer was identified as an independent prognostic factor, which could be incorporated into standard TNM staging system to refine risk stratification and predict for overall survival benefit from postoperative chemotherapy in patients with gastric cancer.

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Effect of increasing radiation dose on pathologic complete response in rectal cancer patients treated with neoadjuvant chemoradiation therapy

Acta Oncol. 2016 Oct 20:1-8.
Hall MD, Schultheiss TE, Smith DD3,, Fakih MG, Wong JY, Chen YJ

BACKGROUND:
Neoadjuvant chemoradiation therapy (CRT) increases pathological complete response (pCR) rates compared to radiotherapy alone in patients with stage II-III rectal cancer. Limited evidence addresses whether radiotherapy dose escalation further improves pCR rates. Our purpose is to measure the effects of radiotherapy dose and other factors on post-therapy pathologic tumor (ypT) and nodal stage in rectal cancer patients treated with neoadjuvant CRT followed by mesorectal excision.
MATERIAL AND METHODS:
A non-randomized comparative effectiveness analysis was performed of rectal cancer patients treated in 2000-2013 from the National Oncology Data Alliance™ (NODA), a pooled database of cancer registries from>150US hospitals. The NODA contains the same data submitted to state cancer registries and SEER combined with validated radiotherapy and chemotherapy records. Eligible patients were treated with neoadjuvant CRT followed by proctectomy and had complete data on treatment start dates, radiotherapy dose, clinical tumor (cT) and ypT stage, and number of positive nodes at surgery (n = 3298 patients). Multivariable logistic regression was used to assess the predictive value of independent variables on achieving a pCR.
RESULTS:
On multivariable regression, radiotherapy dose, cT stage, and time interval between CRT and surgery were significant predictors of achieving a pCR. After adjusting for the effect of other variates, patients treated with higher radiotherapy doses were also more likely to have negative nodes at surgery and be downstaged from cT3-T4 and/or node positive disease to ypT0-T2N0 after neoadjuvant CRT.
CONCLUSION:
Our study suggests that increasing dose significantly improved pCR rates and downstaging in rectal cancer patients treated with neoadjuvant CRT followed by surgery.

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Decreased platelet reactivity in patients with cancer is associated with high risk of venous thromboembolism and poor prognosis

Thromb Haemost. 2016 Oct 20;117(1).
Riedl J, Kaider A, Marosi C, Prager GW, Eichelberger B, Assinger A, Pabinger I, Panzer S, Ay C1

Platelets are suggested to play a crucial role in cancer progression and the prothrombotic state of cancer patients. Here, we aimed to examine the activation status of platelets in cancer patients and investigate their association with risk of death and occurrence of venous thromboembolism (VTE) in a prospective observational cohort study. We measured platelet surface P-selectin, activated glycoprotein (GP) IIb/IIIa and monocyte-platelet aggregate (MPA) formation in vivo and platelet response to ex vivo stimulation with agonists of protease-activated receptor (PAR) -1, -4, and GPVI, by whole blood flow cytometry, before beginning of chemotherapy and repeatedly during the first six months thereafter (total number of samples analysed: 230). Endpoints of the study were occurrence of death or VTE during a two-year follow-up, respectively. Of 62 patients (median age [interquartile range, IQR]: 63 [54-70] years, 48 % female), 32 (51.6 %) died and nine (14.5%) developed VTE. Association with a higher risk of death was found for lower platelet surface expression of P-selectin and activated GPIIb/IIIa in vivo and in response to PAR-1, -4 and GPVI activation, but not for MPA formation. Furthermore, reduced platelet responsiveness to PAR-1 and GPVI agonists was associated with higher risk of VTE (hazard ratio per decile increase of percentage P-selectin positive platelets: 0.73 [0.56-0.92, p=0.007] and 0.77 [0.59-0.98, p=0.034], respectively). In conclusion, cancer patients with a poor prognosis showed decreased platelet reactivity, presumably as a consequence of continuous activation. Our data suggest that decreased platelet reactivity is associated with increased mortality and VTE in cancer.

[Two Cases of Germ Cell Tumors with Hyperthyroidism Due to High Serum hCGLevels]

Hinyokika Kiyo. 2016 Sep;62(9):489-493. doi: 10.14989/ActaUrolJap_62_9_489
[Article in Japanese]
Chihara I, Nitta S, Kimura T, Kandori S, Kawahara T, Waku N, Kojima T, Joraku A, Miyazaki J, Iwasaki H, Suzuki H, Kawai K, Nishiyama H.

We reported two cases of hyperthyroidism that developed during induction chemotherapy for advanced germ cell tumors with high serum human chorionic gonadotropin (hCG) levels. Case 1: An 18-year-old man with mediastinal choriocarcinoma complained of tachycardia and tremor. His pretreatment serum hCG level was 1.37 million mIU/ml. The free thyroxine (fT4) level measured on day 2 of the first course of bleomycin, etoposide and cisplatin (BEP) was elevated to 7.8 ng/dl (<1.7 ng/dl), whereas the thyroid stimulating hormone (TSH) level was undetectable. We diagnosed the patient with hyperthyroidism and started oral propranolol and thiamazole. Subsequently, his tachycardia and tremor disappeared. On day 12 of the first course of BEP, his hCG level decreased to less than 50,000 mIU/ml. Also, his fT4 level returned to the normal range. Case 2 : A 29-year-old man presented with a left scrotal mass. He was diagnosed with non-seminoma testicular cancer (embryonal carcinoma and choriocarcinoma) with multiple lung, liver and lymph node metastases. On the admission day, his serum hCG and fT4 levels were high ; 3.23 million mIU/ml and 2.2 ng/dl, respectively. The TSH level was low at 0.011 mIU/ml. On day 3 of the first course of BEP, his hCG and fT4 levels increased to 4.5 million mIU/ml and 3.0 ng/dl, respectively. He complained of tachycardia, tremor and hyperhydrosis. He was started on propranolol and potassium iodide. After the treatment, histachycardia, tremor and hyperhidrosisdis appeared. HisfT4 level normalized on day 17 of the first course of BEP. The TSH-like activity of hCG is considered to be responsible for paraneoplastic hyperthyroidism among germ cell cancer patients with high hCG levels. To our knowledge, this is the first report of such a case in Japan. However, this phenomenon is not rare among patients with extremely high hCG levels. Therefore, we should be careful of these patients.

Successful treatment of primary advanced gastric plasmacytoma using a combination of surgical resection and chemotherapy with bortezomib: A case report

Int J Surg Case Rep. 2016;27:133-136. doi: 10.1016/j.ijscr.2016.08.041
Fukuhara S, Tazawa H, Okanobu H, Kida M, Kido M, Takafuta T, Nishida T, Ohdan H, Sakimoto H

INTRODUCTION:
Extramedullary plasmacytoma (EMP) is a plasma cell neoplasm that presents as a solitary tumor. EMP in the gastrointestinal organs are extremely uncommon.
PRESENTATION OF CASE:
A 36-year-old man was admitted to our hospital with advanced anemia. He had no specific medical history. Gastroendoscopic findings showed an 8.0-cm submucosal tumor with ulcer on the greater curvature of the gastric body. Fine-needle aspiration was performed, and the pathologic diagnosis of the submucosal tumor was a plasmacytoma. Therefore, the patient was diagnosed with gastric plasmacytoma. A total gastrectomy was performed with lymphadenectomy. The result of intraoperative peritoneal lavage cytology was positive. Histological examination revealed serosa-exposed plasmacytoma of the stomach with lymph nodes metastasis. Additionally the patient received a three-drug chemotherapy regimen (bortezomib, cyclophosphamide, and dexamethasone [VCD]) from 3 weeks after the operation. After 4 cycles of chemotherapy, the patient received autologous peripheral blood stem-cell transplantation (auto-PBSCT). Eighteen months after diagnosis, the patient is in complete remission with no evidence of local relapse or evolution to multiple myeloma.
CONCLUSIONS:
This is the first reported case of advanced gastric plasmacytoma using adjuvant chemotherapy involving bortezomib and auto-PBSCT after the resection, and the patient has maintained a good course over a year. This protocol could be a new way to treat these tumors.

[A cohort study comparing the efficacy and safety of bortezomib plus dexamethasone versus bortezomib, epirubicin and dexamethasone in patients with multiple myeloma]

Zhonghua Nei Ke Za Zhi. 2016 Sep 1;55(9):689-94. doi: 10.3760/cma.j.issn.0578-1426.2016.09.007
[Article in Chinese]
Hao QY, Chen H, Liu KY, Wen L, Huang XJ, Lu J

OBJECTIVE:
Bortezomib plus dexamethasone (BD) and bortezomib, epirubicin plus dexamethasone (PAD) are both front-line regimens of multiple myeloma. This study aimed to assess the efficacy and safety of BD versus PAD regimens in multiple myeloma.
METHODS:
All 208 patients with newly diagnosed multiple myeloma using either BD or PAD front-line regimens were enrolled between November 2006 and July 2014. Front-line chemotherapy regimens were 2-7 cycles. Response rates, overall survival, progression-free survival, and adverse effects were retrospectively analyzed.
RESULTS:
(1) In PAD group, the overall response rate was 82.9% [complete response(CR) 28.6%, very good partial response(VGPR) 12.9%], which was similar as that in BD group [70.3% (CR 26.8%, VGPR 5.1%), P=0.049]. The estimated median progression-free survival was 34.0 months in PAD group versus 25.0 months in BD group (P=0.010). (2) The triplet regimen has a higher accumulated response rate along with chemotherapy cycles, but it didn't show any difference with the doublet regimen. (3) In elderly patients (>65 years old), the overall response rates in two groups had no significant difference (P=0.769), while in patients ≤65 years old, PAD regimen were more effective than BD regimen (P=0.037). (4) Grade 3 and 4 adverse events were recorded with a higher number of patients in the PAD group than those in the BD group.

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CONCLUSIONS:

Compared with BD regimen, PAD regimen improves the initial response rates, especially deep responses, as well as progression-free survival in patients with newly diagnosed multiple myeloma. However, more severe toxicities are accordingly higher. In elderly patients, overall response rate, estimated median progression-free survival, and median overall survival are all comparable in both regimens.

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