Conclusion: Recruiting patients and their relatives and collecting their tumor specimens allows scientists/clinicians to conduct research studies and also to identify those individuals who may benefit from cancer screening for early detection and curative resection.

https://doi.org/10.1016/j.annonc.2022.05.034

O11-1 Prognostic impacts of loss of skeletal muscle mass during neoadjuvant chemotherapy in older esophageal cancer patients

Tsuyoshi Harada[1,2], Tetsuya Tsuji[1,3], Jnnya Ueno[1], You Koishihara[1], Nobuko Konishi[1], Nanako Hijikata[1], Aiko Ishikawa[1,3], Daisuke Kotani[4], Kojima Takashi[4], Hisashi Fujiwara[5], Takeo Fujita[5]

[1]Department of Rehabilitation, National Cancer Center Hospital East, Chiba, Japan; [2]Department of Rehabilitation Medicine, Keio University Graduate School, Tokyo, Japan; [3]Department of Rehabilitation Medicine, Keio University School of Medicine, Tokyo, Japan; [4]Department of Gastrointestinal Oncology, National Cancer Center Hospital East, Chiba, Japan; [5]Department of Esophageal Surgery, National Cancer Center Hospital East, Chiba, Japan

Background: In patients with locally advanced esophageal cancer (EC), the loss of skeletal muscle mass during neoadjuvant chemotherapy (NAC) is reported to impact prognosis. However, it is not revealed in older patients. The aim of this retrospective study is to investigate the impact of the loss of skeletal muscle mass index (SMI) during NAC on prognosis after esophagectomy in older patients.

Methods: Subjects were older patients aged 65 years or older with EC treated with NAC including Docetaxel+CDDP+5-FU and CDDP+5-FU followed by R0 esophagectomy from 2016 to 2020. The change ratio of SMI (SMI%) was calculated with CT images before and after NAC. The cut-off point of SMI% for 3-years overall survival (OS) was defined with the Log-rank test. Cox proportional hazards model was performed for OS. Chi-square test and analysis of variance test were used for investigating characteristics of patients with loss of SMI.

Results: A total of 188 patients (mean age: 71±3 years) treated with NAC was analyzed. Mean SMI% was -6.4±5.7%. The cut-off point of SMI% for OS was defined as -12%. The group with major loss of SMI (n=30) showed a significantly lower OS rate compared with the group with minor loss of SMI (n=158) (OS rate: 61% vs. 79%, p=0.009). The Major reason for death was recurrent EC in both groups (67% and 70%). The major loss of SMI (vs. minor loss of SMI) significantly impacted OS [Hazard ratio 2.467 (95% CI 1.063-5.724), p=0.036], independent of age, sex, pre-NAC sarcopenia, comorbidity, pT and pN stage, histological type, regimen and histological effect of NAC. In addition, the group with major loss of SMI also showed a significantly higher rate of postoperative pneumonia than those with minor loss of SMI (27% vs. 19%, p=0.013).

Conclusion: The loss of SMI during NAC was an independent prognostic factor for OS after esophagectomy. The progression of vulnerability with loss of skeletal muscle mass during NAC may impact survival in older patients.

https://doi.org/10.1016/j.annonc.2022.05.035

O11-3 Usefulness of the MEWS as an ultra-short-term prognosis predictor for patients with gastrointestinal cancer

Tomomi Sanomachi[1,2], Hisatsugu Ohori[1], Takashi Yoshioka[2]

[1]Dept. Clin. Oncol., Japan. Red Cross Ishinomaki Hosp; [2]Dept. Clin. Oncol., Yamagata Univ. Hosp

Objective: Various scoring methods are used for prognosis prediction of cancer patients, but most are limited to medium- to short-term prognosis prediction (few months to few weeks). Daily ultra-short-term prognosis prediction indicators have not yet been established. Prognosis prediction in such cases is often subjectively evaluated based on the signs of near-death, but the modified early warning score (MEWS) is frequently used not only for cancer patients but also in hospitals in Japan and overseas as a numerical index to determine changes in patients' condition. Therefore, we examined the usefulness of MEWS as an index for predicting the ultra-short-term prognosis of patients with gastrointestinal cancer

Methods: Since the inception of the MEWS system in August 2017 until March 2021, multiple logistic regression analysis was performed for 4296 scoring data of 136 patients with gastrointestinal system cancer who died at our hospital. We examined how the MEWS items (blood pressure, body temperature, pulse rate, respiration, and consciousness scores) and factors such as sex and age could contribute to survival and death within 3 days, 2 days, and 1 day of death.

Results: Of the 136 patients, 96 were men and the median age was 68 (range: 26-105) years. There were 31 gastric cancer, 24 colon cancer, 23 pancreatic cancer, and 13 gallbladder/cholangiocarcinoma cases. We found that the shorter the time to death, the higher the prediction accuracy. Three days before death, the regression equation was p = 0.14 according to the Hosmer-Lemeshow test, the area under the curve was 0.81, and the fitness could be guaranteed. The contributions of consciousness (0.38) and blood pressure (0.52) were particularly high based on the odds ratio.

Conclusion: Utilization of MEWS considering the sex and age of patients with gastrointestinal cancer may be sufficiently useful as an ultra-short-term prognosis prediction index within 3 days of death.

https://doi.org/10.1016/j.annonc.2022.05.036

O12-1 Ramucirumab-containing chemotherapy for gastrointestinal neuroendocrine carcinoma: RAM-NEC study (WJOG13420G)

Yuki Matsubara[1], Toshiki Masuishi[1], Hidekazu Hirano[2], Saori Mishima[3], Mitsuhiro Furuta[4], Tomoyuki Otsuka[5], Kenta Kawasaki[6], Takeshi Kawakami[7], Kazuhiro Yanagihara[8], Takaya Shimura[9], Masato Komoda[10], Kozue Murayama[11], Keiko Minashi[12], Yoshiyuki Yamamoto[13], Yudai Shinohara[14], Shinichi Nishina[15], Nobuyuki Musha[16], Kyoko Kato[17], Isao Oze[18], Kei Muro[1]

[1]Department of Clinical Oncology, Aichi Cancer Center Hospital; [2]Department of Gastrointestinal Medical Oncology, National Cancer Center Hospital; [3]Department of Gastroenterology and Gastrointestinal Oncology, National Cancer Center Hospital East; [4]Division of Gastroenterology, Kanagawa Cancer Center; [5]Department of Medical Oncology, Osaka International Cancer Institute; [6]Division of Gastroenterology and Hepatology, Department of Internal Medicine, Keio University School of Medicine; [7]Gastrointestinal Oncology, Shizuoka Cancer Center Hospital; [8]Department of Medical Oncology, Kansai Electric Power Hospital; [9]Department of Gastroenterology and Metabolism, Nagoya City University Graduate School of Medical Sciences; [10]Department of Gastrointestinal and Medical Oncology, National Kyushu Cancer Center; [11]Department of Gastroenterology, Saitama Cancer Center; [12]Clinical Trial Promotion Department, Chiba Cancer Center; [13]Department of Gastroenterology, Faculty of Medicine, University of Tsukuba; [14]Department of Hematology/Oncology, Japan Community Healthcare Organization Kyushu Hospital; [15]Department of Medical Oncology, Kurashiki Central Hospital; [16]Department of Surgery, Saiseikai Niigata Hospital; [17]Department of Medical Oncology, National Hospital Organization Nagoya Medical Center; [18]Division of Cancer Epidemiology and Prevention, Aichi Cancer Center Research Institute

Background: Second-line chemotherapy (CTx) for advanced gastrointestinal neuroendocrine carcinoma (GI-NEC) after platinum-based CTx is adopted according to the guidelines of GI adenocarcinoma or small cell lung cancer in daily practice. Recently, some reports suggested that vascular endothelial growth factor receptor-2 highly expressed in tumor vessels of GI-NEC. In this study, we evaluated the efficacy of ramucirumab (RAM)-containing CTx.

Methods: We retrospectively evaluated gastric (G-) or colorectal (C-) NEC patients (pts) previously treated with platinum-based CTx followed by second-line CTx between March 2015 and June 2020 (G-NEC) or between May 2016 and June 2020 (C-NEC). We compared the efficacy of RAM-containing CTx as second- or later-line treatment (Group A) with that of CTx without RAM as second-line treatment (Group B). A Cox proportional hazard model and propensity scores were used for statistical analysis.

Results: From 25 facilities, 139 pts were included. Group A and B contained 50 (G/C, 43/7 pts) and 89 (G/C, 58/31 pts) pts, respectively. Pt characteristics were as follows (Group A/B): median age, 70/68; ECOG PS 1-2, 66/69%, more than two prior regimens, 46/0%. The CTx in combination with RAM in Group A was paclitaxel/nab-paclitaxel/FOLFIRI (62/26/12%). Second-line CTx in Group B were commonly amrubicin (58%) and irinotecan (11%). The efficacy (Group A/B) were as follows: median overall survival (mOS), 8.6/5.8 months (mo) (HR, 0.68; 95% CI, 0.45-1.01; $p = 0.058$); median progression-free survival, 4.3/1.9 mo (HR, 0.57; 95% CI, 0.39-0.84; $p = 0.004$); objective response rate, 50/8% ($p < 0.0001$); mOS in G-NEC, 8.6/5.3 mo (HR, 0.62; $p = 0.047$); and mOS in C-NEC, 5.4/6.8 mo (HR, 0.66; $p = 0.378$). The most common grade 3 or higher treatment-related adverse event that occurred in more than 5% of pts in Group A was neutropenia (32%).

Conclusion: This study suggests that RAM-containing CTx as second- or later-line treatment is effective for G- or C-NEC pts.

https://doi.org/10.1016/j.annonc.2022.05.037

O12-2 The epidemiology of rare cancers from National Cancer Registry in Japan

Tomoyuki Satake[1], Chigusa Morizane[1], Ryoko Rikitake[2], Shintaro Iwata[3], Hidekazu Hirano[4], Dai Ogata[5], Tatsunori Shimoi[6], Kazuki Sudo[6], Seiichi Yoshimoto[7], Naoya Yamazaki[5], Yoko Katoh[8], Takahiro Higashi[2], Akira Kawai[3]

[1]Department of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital; [2]Division of Health Services Research, Institute for Cancer Control, National Cancer Center; [3]Department of Musculoskeletal Oncology and Rehabilitation, National Cancer Center Hospital; [4]Department of Gastrointestinal Medical Oncology, National Cancer Center Hospital; [5]Department of Dermatologic Oncology, National Cancer Center Hospital; [6]Department of Medical Oncology, National Cancer Center Hospital; [7]Department of Head and Neck Surgery, National Cancer Center Hospital; [8]Rare Cancer Center, National Cancer Center

Background: Rare cancers are defined as malignancies with an incidence of less than 6 per 100,000 people per year. Approximately 200 different malignancies are categorized as rare cancers, and 15% of all malignancies are represented by rare cancers

in Japan. However, epidemiological information, including the incidents, distribution of age, sex, region, were mainly estimated by hospital-based cancer registry and organ-specific cancer registries, and comprehensive actual numbers were insufficient. Especially in rare cancers, the reliability of the estimated epidemiological data may be unstable, because of rarity of disease. We aimed to elucidate these features of rare cancers using National Cancer Registry (NCR) in Japan.

Methods: We extracted information from data submitted to NCR in Japan from 2016 to 2017. We used histologic codes from the International Classification of Diseases for Oncology, 3rd Edition. We selected primary organs with particularly high unmet medical needs and extracted epidemiological data on rare histological types of each organ.

Results: Epidemiological data of over 100,000 patients with rare cancers were obtained, including rare histological subtypes arising from breast, gynecologic organs, urologic organs, bone and soft tissue, hepatobiliary and pancreas, skin, head and neck, gastrointestinal GISTs, and others. We investigated sex, age, disease stage, primary treatment types, and role of designated cancer care hospitals for rare cancers. Overview of our project and part of the results will be shown at the conference.

Conclusion: Our study revealed the epidemiology of rare cancers in Japan, and those data are important reference for clinical practice and future studies. NCR was useful to understand overall pictures of rare cancers.

https://doi.org/10.1016/j.annonc.2022.05.038

O12-3 Comprehensive significance of cancer genomic profiling (CGP) tests in patients with advanced skin cancers

Dai Ogata[1], Yoshiyuki Matsui[1], Akira Takahashi[1], Kenjiro Namikawa[1], Kuniko Sunami[3], Takafumi Koyama[2], Naoya Yamazaki[1]

[1]Department of Dermatologic Oncology, National Cancer Center Hospital; [2]Department of experimental therapeutics, National Cancer Center Hospital; [3]Department of Clinical Laboratory, National Cancer Center Hospital

Background: Skin cancer is a rare cancer, with very limited approved drugs. In particular, none of the drugs have been approved for basal cell carcinoma (BCC) and adnexal carcinoma.

Since June 2019, Comprehensive genomic profiling (CGP) tests have been reimbursed by the National Health Insurance system in Japan, with restrictions for government-designated hospitals with a molecular tumor board composed of multidisciplinary specialists, known as an expert panel (EP). We aimed to reveal how effectively CGP is utilized for skin cancer.

Methods: We retrospectively analyzed data of 60 patients with skin cancers who underwent either of the two CGP tests (the OncoGuide NCC Oncopanel System and the FoundationOne CDx Cancer Genomic Profile) at National Cancer Center Hospital. Data on consecutive cases who underwent the CGP tests at our department between August 2019 and July 2021 were collected. We evaluated the proportions of cases that received genomically matched treatments, including investigational new drugs based on CGP results.

Results: All 60 patients had appropriate results. median age was 60.5 years (range 8-89), Male: Female ratio 35:25. Among them, malignant melanoma (MM) was 60% (n=36), adnexal carcinoma (AC) was 23% (n=14), squamous cell carcinoma (SCC) was 12% (n=7), BCC was 3% (n=2) and merkel cell carcinoma (MCC) was 2% (n=1), respectively. Actionable gene alterations were identified in 28 patients (47%). The most commonly affected genes were BRAF, NF1, NRAS and TP53 in MM: ERBB2 in AC. Other than that, it varied from case to case. As a result, 28 patients were provided with information for genomically matched therapies and 15 (25%) could be received them. This result was higher than previously reported for other solid tumors.

Discussion: Incorporating the publicly reimbursed CGP tests into skin cancer management could allow for more precise sub-classification of these rare disease, as well as personalized matching of patients to therapies.

https://doi.org/10.1016/j.annonc.2022.05.039

O12-4 Clinical significance of comprehensive genomic profiling in pediatric cancer patients

Minako Sugiyama[1,5], Junko Kikuchi[1], Yoshihito Ohhara[2], Kanako Hagio[1], Toraji Amano[2], Emi Takakuwa[3], C. Kanako Hatanaka[4], Yutaka Hatanaka[4], Atsushi Manabe[5], Takeo Sarashina[6], Masaki Yamamoto[7], Yusuke Mizukami[8], Kohichi Takada[9], Hirohiro Naruse[10], Takashi Mitamura[11], Ichiro Yabe[11], Akihiro Sakurai[12], Hirotoshi Dosaka-Akita[2], Ichiro Kinoshita[1]

[1]Division of Clinical Cancer Genomics, Hokkaido University Hospital; [2]Department of Medical Oncology, Hokkaido University Hospital; [3]Department of Surgical Pathology, Hokkaido University Hospital; [4]Center for Development of Advanced Diagnostics, Hokkaido University Hospital; [5]Department of Pediatrics, Hokkaido University Hospital; [6]Department of Pediatrics, Asahikawa Medical University Hospital; [7]Department of Pediatrics, Sapporo Medical University; [8]Genetic Oncology Department, Asahikawa Medical University Hospital; [9]Department of Medical Oncology, Sapporo Medical University; [10]Department of Gastroenterology, Hakodate Municipal Hospital, Hakodate; [11]Division of Clinical Genetics, Hokkaido University Hospital; [12]Department of Medical Genetics and Genomics, Sapporo Medical University

Background: Since June 2019, gene alterations in patients (pts) with advanced solid cancers are screened on comprehensive genomic profiling (CGP) tests, which is covered by the national health insurance system in Japan. Although most of the molecular-targeted drugs corresponding to the actionable genes alterations in solid cancers are off-labeled in pediatric pts, their therapeutic efficacy may be superior to conventional anticancer drugs.

Methods: We analyzed the data of 25 pediatric pts who had CGP results discussed in the expert panel at Hokkaido University Hospital between June 2019 and July 2021.

Results: The median age at the examination was eight years ranging from six months to 20 years. Eight of 25 pts had a central nervous tumor. Nineteen pts received FoundationOne CDx (F1 CDx), and 6 pts received OncoGuide NCC Oncopanel (NCC Oncopanel). Actionable gene alterations were identified in 21 pts (21/25, 84%), and 5 pts (5/25, 20%) received genotype-matched therapies. A patient (pt) with ovarian carcinoma with loss of heterozygosity score received chemotherapy, including cisplatin, and a pt with infantile fibrosarcoma with LMNA-NTRK1 fusion received entrectinib. The two pts had achieved complete response. A pt with juvenile xanthogranuloma and a pt with rhabdomyosarcoma with ALK fusion received ALK-inhibitors. The two pts had achieved partial response. A pt with pilocytic astrocytoma having BRAF V600E alteration just started a combination therapy of BRAF inhibitor and MEK inhibitor. Therefore, all the four evaluable pts achieved significant tumor response. In addition, two pathogenic germline variants by NCC Oncopanel and 6 presumable pathogenic germline variants by F1 CDx were revealed. Four of the eight variants were SMARCB1 in rhabdoid tumors. Finally, two of the eight pts were diagnosed with Li Fraumeni syndrome.

Conclusion: CGP tests for pediatric cancer pts are feasible and may lead to the significant therapeutic efficacy of genotype-matched therapy.

https://doi.org/10.1016/j.annonc.2022.05.040

O12-5 A retrospective analysis of the clinical factors affecting the prognosis of non-seminomatous mediastinal germ cell tumor

Yosuke Amano, Tatsunori Shimoi, Momoko Tokura, Chiharu Mizoguchi, Shosuke Kita, Kasumi Yamamoto, Shu Yazaki, Hitomi Okuma, Yuki Kojima, Tadaaki Nishikawa, Emi Noguchi, Kazuki Sudo, Kan Yonemori

Department of Medical Oncology, National Cancer Center Hospital

Introduction: International Germ Cell Cancer Consensus Group (IGCCCG) updated the prognosticators in germ cell tumors (GCTs) in 2021. However, since the proportion of mediastinal GCTs in the registry was low, it is uncertain whether these prognosticators can apply to mediastinal GCTs.

Methods: We retrospectively analyzed the clinical factors including new IGCCCG prognostic factors affecting the prognosis of mediastinal non-seminomatous GCSs in National Cancer Center Hospital (NCCH).

Results: Among 91 cases with mediastinal GCTs treated in NCCH during January 2001 to June 2021, 29 were seminoma and 62 were non-seminomatous GCTs. Three-year relapse free survival (RFS) rate and three-year overall survival (OS) rate were 96.6% (95% CI 77.9-99.5%) and 96.6% (95% CI 77.9-99.5%) in seminoma, 58.6% (95% CI 45.1-69.9%) and 72.5% (95% CI 58.4-82.6%) in non-seminomatous GCTs, respectively. In cases with nonseminomatous GCTs, age, lactate dehydrogenase, alpha-fetoprotein or human chorionic gonadotropin did not affect the prognosis significantly among IGCCCG prognosticators. Univariate survival analysis using log-rank test revealed that the presence of lung metastasis (RFS HR 3.38, $p = 0.002$; OS HR 2.81, $p = 0.043$), extrapulmonary metastasis (RFS HR 5.95, $p < 0.001$; OS HR 8.38, $p < 0.001$), pleural effusion (RFS HR 2.30, $p = 0.029$; OS HR 4.53, $p = 0.001$), and elevation of D-dimer (RFS HR 2.96, $p = 0.019$; OS HR 4.07, $p = 0.021$) significantly deteriorated relapse-free survival and overall survival. Additionally, in cases receiving surgical resection after chemotherapy, pathological complete response except teratoma component could predict better prognosis significantly (RFS HR 0.11, $p < 0.001$; OS HR 0.13, $p = 0.004$).