



P3.379: Genomic Landscape of Pleural Mesothelioma in Japanese Patients, a Comprehensive Analysis Using Nationwide Database

Hirokazu Taniguchi^{1,2}, Kazumasa Akagi^{1,2}, Takahito Fukuda², Takuya Honda^{1,3}, Hirokazu Kurohama⁴, Nozomi Ueki⁴, Yuki Matsuo⁴, Emiko Udo⁵, Saya Yahata⁵, Shoko Miura⁶, Hiromi Tomono², Noritaka Honda², Yosuke Dotsu², Midori Matsuo^{2,7}, Shinnosuke Takemoto², Izumi Sato⁸, Shinji Okano⁹, Masahiro Nakashima⁴, Hiroshi Mukae², Kazuto Ashizawa^{1,10}

1 Clinical Oncology Center, 2 Department of Respiratory Medicine, 3 Department of Gastroenterology and Hepatology, 4 Department of Tumor and Diagnostic Pathology, 5 Cancer Genomics Unit, Clinical Genomics Center, 6 Department of Obstetrics and Gynecology, 7 Clinical Research Center, 8 Department of Clinical Epidemiology, 9 Department of Pathology, 10 Department of Clinical Oncology, Nagasaki University, Nagasaki, Japan.



INTRODUCTION

Pleural mesothelioma (PM) is a rare and aggressive malignancy primarily associated with asbestos exposure. Although immune checkpoint inhibitors (ICIs) and platinum-based chemotherapy have improved outcomes, treatment options remain limited, and drug development is challenging because of the rarity of PM. PM is characterized by frequent alterations in tumor suppressor genes, including *BAP1*, *CDKN2A*, and *NF2*, which are difficult to target directly. Large-scale genomic studies, including The Cancer Genome Atlas (TCGA), have clarified the molecular landscape of PM; however, Asian patients have been underrepresented. Given reported ethnic differences in oncogenic alterations in other cancers, the genomic characteristics of PM may also differ across populations. Thus, genomic data on Japanese patients with PM remain limited. In Japan, comprehensive genomic profiling (CGP) has been covered by national insurance since 2019. The Center for Cancer Genomics and Advanced Therapeutics (C-CAT) integrates genomic and detailed clinical data from CGP testing nationwide, providing a unique real-world resource for cancer genomic medicine. This study aimed to characterize the genomic alterations and clinical features of Japanese patients with PM registered in C-CAT and to explore potential ethnic differences through comparison with publicly available datasets, including TCGA.

METHODS

Study design and data source

This retrospective nationwide cohort study used clinical and genomic data from C-CAT database in Japan. Patients with PM who underwent CGP between June 2019 and March 2025 were included. Genomic data generated by different CGP platforms were standardized by C-CAT.

Study patients and data items/definitions

Clinical variables included age, sex, performance status, smoking history, histological subtype, CGP test type, and treatment history. Genomic variables included single-nucleotide variants, copy number alterations, gene rearrangements, tumor mutation burden (TMB), and microsatellite instability. Histological and treatment records were reviewed for consistency. Patients receiving nivolumab, ipilimumab, atezolizumab, or pembrolizumab were classified as having received ICIs.

Statistical analysis

Overall survival (OS) was estimated using the Kaplan–Meier method and compared by ICI exposure, histologic subtype, TMB status, and major gene alterations using log-rank tests. Genes altered in fewer than 10 patients were excluded. Prognostic factors were assessed using univariate and multivariate Cox proportional hazards models. For external comparison, TCGA-MESO somatic mutation data were retrieved using TCGAbiolinks and compared with the C-CAT cohort. Analyses were performed in R version 4.5.0, with two-sided $p < 0.05$ considered significant.

DISCUSSION and CONCLUSION

- ✓ This study showed the genetic alterations associated with PM in Japanese patients by analyzing a large-scale clinical-genomic database, C-CAT. This represents one of the largest cohorts to date in which genomic data on PM have been integrated with detailed clinical information.
- ✓ The most frequently observed gene mutations were *BAP1*, *NF2*, *NOTCH3*, *TP53*, and *STK11* and copy number alternations were losses of *CDKN2A*, *CDKN2B*, *MTAP*, *BAP1*, and *TEK* in Japanese patients with PM.
- ✓ TMB and TP53 expression were suggested as potential prognostic factors in Japanese patients with PM. Our findings confirmed that PM typically harbors a low TMB. Using a cutoff value of 1.6, patients with a higher TMB had worse survival rates. *TP53* alterations as an indicator of poor prognosis were seen in various malignancies.
- ✓ Although actionable genetic alterations that are directly targeted by existing drugs are limited, our findings suggest the potential of several factors as clinically relevant biomarkers.
- ✓ Further studies are warranted to facilitate the development of novel therapeutic agents that may improve the survival outcomes of patients with PM.

Study Limitations:

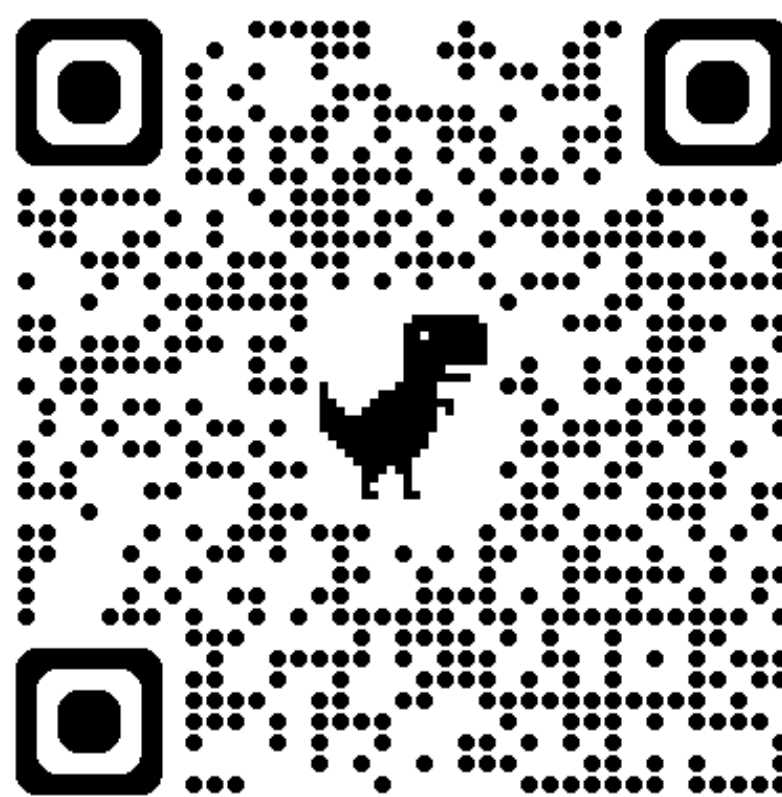
- A retrospective database analysis
- Risk of selection bias in patients undergoing CGP testing
- CGP assays used in Japan are based on targeted sequencing
- Unable to evaluate clonal hematopoiesis of indeterminate potential

REFERENCES & ACKNOWLEDGEMENTS

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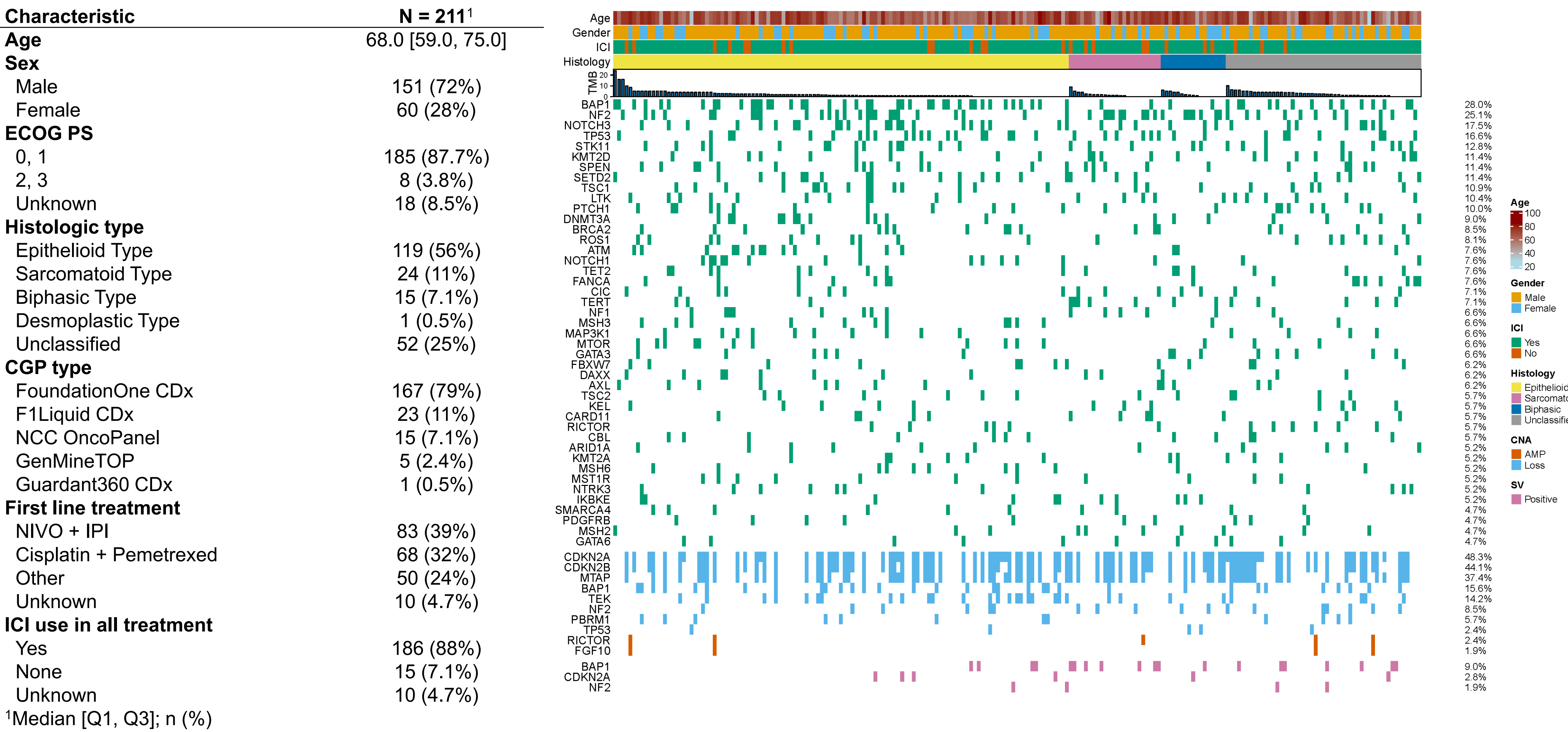
No AI was used in this study

Further detailed information is available from the QR code.



RESULTS

Patient characteristics and Genomic landscape of pleural mesothelioma in C-CAT



Overall survival based on clinical characteristics and genomic alterations.

