

厚生労働行政推進調査事業費補助金（肝炎等克服政策研究事業）
分担研究報告書

肝がん・重度肝硬変の医療水準と患者のQOL向上等に資する研究

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データ収集プラットフォーム整備

A 研究目的

肝癌に対する免疫療法と局所治療の組み合わせの効果と安全性を検証する事。特に各国の研究状況と成績における実態調査を行う事。

B 研究方法

肝癌に対する各種国際学会に出席し発表を行うとともに、海外のデータについても日本との成績と比較検討する。

C 研究結果

日本の肝癌における複合免疫療法と局所治療の組み合わせが海外とはアプローチ方法が異なり、最も優れている事が判明した。

D 考察

今後日本において、肝癌の治療を効率的に進めるには複合免疫療法の経済的サポートと共に局所治療と組み合わせる事が重要と考えられた。

E 結論

日本の肝癌の治療、特に複合免疫療法による治療成績は海外より優っていると考えられた。これについては、日本独自の局所治療との組み合わせは極めて重要であると考えられた。

F 健康危険情報

なし

G 研究発表

1.論文発表

1. Kudo M*: The Society for Immunotherapy of Cancer clinical practice guideline on immunotherapy for hepatocellular carcinoma. Hepatobiliary Surg Nutr 12:256-260,2023.
2. Kudo M*: Adjuvant atezolizumab-bevacizumab after curative therapy for hepatocellular carcinoma. Hepatobiliary Surg Nutr 12:435-439,2023.
3. Kudo M*: Adjuvant atezolizumab-bevacizumab after resection or ablation for hepatocellular carcinoma. Liver Cancer 12:189-197,2023.
4. Kudo M*, Finn RS, Galle PR, Zhu AX, Ducreux M, Cheng AL, Ikeda M, Tsuchiya K, Aoki K, Jia J, Lencioni R: IMbrave 150: Efficacy and safety of atezolizumab plus bevacizumab vs sorafenib in patients with Barcelona Clinic Liver Cancer stage B unresectable hepatocellular carcinoma: an exploratory analysis of the Phase III study. Liver Cancer 12:238-250, 2023.
5. Kudo M*: All stages of hepatocellular carcinoma patients benefit from systemic

- therapy combined with locoregional therapy. Liver Cancer 12:395-404, 2023.
6. Kudo M*, Finn RS, Cheng AL, Zhu AX, Ducreux M, Galle PR, Sakamoto N, Kato N, Nakano M, Jia J, Vogel A: Albumin-bilirubin grade analyses of atezolizumab plus bevacizumab vs sorafenib in patients with unresectable hepatocellular carcinoma: A post hoc analysis of the Phase III IMbrave150 study. Liver Cancer 12:479-493, 2023.
 7. Kudo M*: Drug-off criteria in patients with hepatocellular carcinoma who achieved clinical complete response after combination treatment with immunotherapy and locoregional therapy. Liver Cancer 12:289-296, 2023.
 8. Kudo M*, Aoki T, Ueshima K, Tsuchiya K, Morita M, Chishina H, Takita M, Hagiwara S, Minami Y, Ida H, Nishida N, Ogawa C, Tomonari T, Nakamura N, Kuroda H, Takebe A, Takeyama Y, Hidaka M, Eguchi S, Chan SL, Kurosaki M, Izumi N: Achievement of complete response and drug-free status by atezolizumab plus bevacizumab combined with or without curative conversion in patients with transarterial chemoembolization-unstable, intermediate-stage hepatocellular carcinoma: A multicenter proof-of-concept study. Liver Cancer 12:321-338, 2023.
 9. Qin S[†], Chen M[†], Cheng AL[†], Kaseb AO[†], Kudo M[†], Lee HC[†], Yopp AC, Zhou J, Wang L, Wen X, Heo J, Tak WY, Nakamura S, Numata K, Uguen T, Hsiehchen D, Cha E, Hack SP, Lian Q, Ma N, Spahn JH, Wang Y, Wu C, Chow PKH, for the IMbrave050 investigators: Atezolizumab plus bevacizumab versus active surveillance in patients with resected or ablated high-risk hepatocellular carcinoma (IMbrave050): a randomised, open-label, multicentre, phase 3 trial. Lancet 402:1835-1847, 2023. ([†]Shard 1st authors)
 10. Kudo M*: Current therapeutic strategies for hepatocellular carcinoma in Japan. Liver Cancer 12:497-509, 2023.
 11. Abou-Alfa GK[†], Lau G[†], Kudo M[†], Chan SL[†], Kelly RK, Furuse J, Sukepaisarnjaroen W, Kang YK, Dao TV, De Toni EN, Rimassa L, Breder V, Vasilyev A, Heurgue A, Tam VC, Mody K, Thungappa SC, Ostapenko Y, Yau T, Azevedo S, Varela M, Cheng AL, Qin S, Galle PR, Ali S, Gupta C, Makowsky M, Kurland JF, Negro A, Sangro B, fro the HIMALAYA Investigators: Plain language summary of results from the HIMALAYA study: tremelimumab and durvalumab for the treatment of participants with unresectable hepatocellular carcinoma(liver cancer). Future Oncol 19:2505-2516, 2023. ([†]Shard 1st authors)
 12. Kudo M*, Tsuchiya K, Shao YY, Finn RS, Galle PR, Ducreux M, Cheng AL, Yamashita T, Koga H, Take R, Yamada K, Asakawa T, Nakagawa Y, Ikeda M: Impact of bevacizumab being skipped due to adverse events of special interest for bevacizumab in patients with unresectable hepatocellular carcinoma treated with atezolizumab plus bevacizumab: An exploratory analysis of the Phase III IMbrave150 study. Liver Cancer, 2023 (Epub ahead of print). DOI: 10.1159/000535501

2.学会発表

1. 西田直生志, 工藤正俊: B-mode 超音波検査による肝腫瘍診断を支援する人工知能の開発. シンポジウム 3「消化器診療における AI の現状と展望」, 第 109 回日本消化器病学会総会, 令和 5 年 4 月 6-8 日, 出島メッセ長崎, 長崎.
2. 工藤正俊, 金子周一, 熊田博光: 進行性肝細胞癌患者に対するレンバチニブとペム

- プロリズマブ併用療法をレンバチニブ単独療法と比較する第 III 相試験 (LEAP-002)：日本人集団の結果. ワークショッピング「肝癌における薬物療法の最前線」, 第 59 回日本肝臓学会総会, 令和 5 年 6 月 15-16 日, 奈良県コンベンションセンター, JW マリオット・ホテル奈良, 奈良.
3. 工藤正俊, Nakamura S, Numata K, Chen M, Cheng AL, Chow P, Kaseb A, Lee HC, Yopp A, Zhou J, Wang L, Wen X, Heo J, Tak WY, Uguen T, Hsiehchen D, Hack S, Lian Q, Spahn J, Qin S: IMbrave050: 肝細胞癌における切除・焼灼後の Atezo+Bev 療法の有用性を検証する多施設共同第 III 相臨床試験. ワークショッピング 1「肝細胞癌のコンビネーション治療－術前・術後治療－」, 第 59 回日本肝癌研究会, 令和 5 年 7 月 27-28 日, 大阪国際会議場, 大阪.
 4. 西田直生志, 工藤正俊: 超音波診断を支援する人工知能モデルによる肝内胆管癌の鑑別. ワークショッピング 4 「肝腫瘍診療における AI/IT の可能性」, 第 59 回日本肝癌研究会, 令和 5 年 7 月 27-28 日, 大阪国際会議場, 大阪.
 5. Kudo M, Finn RS, Meyer T, Boisserie F, Li S, Chen Y, Abdrashitov R, Zhu AX, Vogel A, Qin S: Impact of risk factors on overall survival (OS) in patients (pts) with unresectable hepatocellular carcinoma (HCC) treated with first-line (1L) tislelizumab (TIS). Annual Meeting of the American Society of Clinical Oncology (ASCO) 2023, Chicago, USA, June 2-6, 2023.
 6. Kudo M, Chen M, Chow PKH, Kaseb AO, Lee HC, Yopp AC, Becker L, Painter SH, Kovic B, Lian Q, Ma N, Wu C, Qin S, Cheng AL: Efficacy, safety and patient reported outcomes (PROs) from the phase III IMbrave050 trial of adjuvant atezolizumab (atezo) + bevacizumab (bev) vs active surveillance in patients with hepatocellular carcinoma (HCC) at high risk of disease recurrence following resection or ablation. Annual Meeting of the American Society of Clinical Oncology (ASCO) 2023, Chicago, USA, June 2-6, 2023.
 7. Kudo M, Vogel A, Meyer T, Boisserie F, Li S, Abdrashitov R, Chen Y, Zhu AX, Qin S, Finn RS: Impact of baseline liver function on overall survival (OS) and safety in patients with unresectable hepatocellular carcinoma (HCC) treated with first-line (1L) tislelizumab: Results from the RATIONALE-301 study. EASL Congress 2023, Vienna, Austria, June 21-24, 2023.
 8. Kudo M, Finn RS, Meyer T, Boisserie F, Li S, Chen Y, Abdrashitov R, Zhu AX, Vogel A, Qin S: Impact of risk factors on overall survival (OS) in patients (pts) with unresectable hepatocellular carcinoma (HCC) treated with first-line (1L) tislelizumab (TIS). Asia-Pacific Gastroenterology Cancer Summit, Academia, Singapore, August 25-26, 2023.
 9. Kudo M, Ueshima K, Tsuchiya K, Kato N, Yamashita T, Shimose S, Numata K, Kodama Y, Tanaka Y, Kuroda H, Itoh S, Aikata H, Hiraoka A, Moriguchi M, Wada Y, Nakao K, Tateishi R, Ogasawara S, Yamamoto K, Ikeda M: Efficacy and safety analysis of a phase II study of atezolizumab plus bevacizumab for TACE-unsuitable patients with tumor burden beyond up-to-seven criteria in intermediate-stage hepatocellular carcinoma: REPLACEMENT study. ILCA 2023, Amsterdam, The Netherlands, September 7-9, 2023.
 10. Kudo M, Aoki T, Ueshima K, Tsuchiya K, Morita M, Chishina H, Takita M, Hagiwara S, Minami Y, Ida H, Nishida N, Ogawa C, Tomonari T, Nakamura N, Kuroda H, Takebe A, Takeyama Y, Hidaka M, Eguchi S, Chan SL,

- Kurosaki M, Izumi N: Achievement of cancer and drug-free status by atezolizumab plus bevacizumab followed by curative conversion in patients with TACE-unsuitable, intermediate-stage HCC: a multicenter proof-of-concept study. ILCA 2023, Amsterdam, The Netherlands, September 7-9, 2023.
11. Kudo M, Hiraoka A, Takayama T, Takikawa Y, Li S, Abd rashitov R, Chen Y, Boisserie F, Ohkawa K, Satoh T: Tislelizumab versus sorafenib in first-line treatment of unresectable hepatocellular carcinoma (HCC): RATIONALE-301 Japanese subpopulation. The 61st Annual Meeting of Japan Society of Clinical Oncology (JSCO 2023), Yokohama, Japan, October 19-21, 2023.
12. Kudo M, Yamashita T, Finn RS, Galle P, Ducreux M, Cheng AL, Tsuchiya K, Sakamoto N, Hige S, Take R, Yamada K, Asakawa T, Nakagawa Y, Ikeda M: IMbrave150: Exploratory analyses for investigating associations between Last update: 22-11-2023 12:00:52pm Final Programme overall survival (OS) and depth of response (DpR) or duration of response (DoR) in patients (pts) with unresectable hepatocellular carcinoma (HCC). ESMO-Asia 2023, Singapore, December 1-3, 2023.
13. Kudo M, Kato N, Kondo S, Inaba Y, Ueshima K, Sasaki M, Ogasawara S, Sahara T, Li S, Shen J, Kimura T, Dutta L, Tamai T, Ikeda M: Analysis of tumor biomarkers in patients (pts) with advanced hepatocellular carcinoma (HCC) from a phase 1b study of E7386, a CREB-binding protein/β-catenin interaction inhibitor, in combination with lenvatinib. ASCO Gastrointestinal Cancers Symposium (ASCO-GI 2024), Moscone West, San Francisco, January 18-20, 2024
- H 知的財産権の出願・登録状況（予定を含む）
1.特許取得：なし
2.実用新案登録：なし
3.その他：なし