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EPICS CONGRESS COVERAGE: ESMO 2020 – FOCUS ON MELANOMA

September 2020

FACULTY EXPERTS

Chair
Jeffrey S. Weber, MD, PhD

Reinhard Dummer, MD

Alexander Eggermont, MD, PhD

James Larkin, MD, PhD

Caroline Robert, MD, PhD

AGENDA

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Time CEST	Topic	Speaker/Moderator
17.30 – 17.35	Introduction and Review Agenda and Framework for Meeting	Jeffrey S. Weber, MD, PhD
17.35 – 17.45	Melanoma Adjuvant and Neoadjuvant Therapy	Alexander Eggermont, MD, PhD
17.45 – 18.05	Key Questions and Topics for Discussion	Moderator: Jeffrey S. Weber, MD, PhD
18.05 – 18.15	Relapsed/Refractory Metastatic Melanoma	Caroline Robert, MD, PhD
18.15 – 18.35	Key Questions and Topics for Discussion	Moderator: Jeffrey S. Weber, MD, PhD
18.35 – 18.45	Immunotherapy for 1L Metastatic Melanoma	Reinhard Dummer, MD
18.45 – 19.05	Key Questions and Topics for Discussion	Moderator: Jeffrey S. Weber, MD, PhD
19.05 – 19.15	BREAK	
19.15 – 19.25	1L *BRAF*-Mutated Metastatic Melanoma – Long-term Results and Strategies to Improve on MAPK-Targeted Therapies	James Larkin, MD, PhD
19.25 – 19.45	Key Questions and Topics for Discussion	Jeffrey S. Weber, MD, PhD
19.45 – 20.00	Summary, Key Takeaways, and Closing Remarks	Jeffrey S. Weber, MD, PhD

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Melanoma Adjuvant and Neoadjuvant Therapy

ALEXANDER EGGERMONT, MD, PHD

1076O: Adjuvant nivolumab (NIVO) vs ipilimumab (IPI) in resected stage III/IV melanoma: 4-y recurrence-free and overall survival (OS) results from CheckMate 238. J. Weber, et al

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Background

> NIVO has shown improved recurrence-free survival (RFS) vs IPI in patients (pts) with resected stage III/IV melanoma in the phase III

LBA46: Pembrolizumab versus placebo after complete resection of high-risk stage III melanoma: Final results regarding distant metastasis-free survival from the EORTC 1325-MG/Keynote 054 double-blinded phase III trial. A. Eggermont, et al

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Background

> The randomized phase III double-blind EORTC 1325/KEYNOTE-054 trial was conducted to evaluate pembrolizumab (PEMBRO) vs placebo

1097P: 4-year relapse-free survival (RFS), overall survival (OS) and long-term toxicity of (neo)adjuvant ipilimumab (IPI) + nivolumab (NIVO) in macroscopic stage III melanoma - OpACIN trial. J.M. Versluis, et al

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Background

> Neoadjuvant (neoadj) IPI + NIVO showed in different trials in almost 200 pts a pathologic response rate of 71%–78%. The

1085P: Health-Related Quality of Life in Stage III Melanoma Patients Treated with Neoadjuvant Ipilimumab and Nivolumab Followed by Index Lymph Node Excision Only versus Therapeutic Lymph Node Dissection: 24 week results of the PRADO trial. N.M.J. Van Den Heuvel, et al

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Background

1100P: Restricted mean survival time (RMST) and cure-rate modeling in estimating survival benefit with adjuvant dabrafenib (D) plus trametinib (T) treatment in melanoma. J.M. Kirkwood, et al

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Background

MELANOMA ADJUVANT AND NEOADJUVANT THERAPY – DISCUSSION (1/3)

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- There was enthusiasm about the results of the PRADO trial (neoadjuvant IPI + NIVO; 1085P) in pts

MELANOMA ADJUVANT AND NEOADJUVANT THERAPY – DISCUSSION (2/3)

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- The following recommendations were made for a neoadjuvant trial design with a sentinel node-

MELANOMA ADJUVANT AND NEOADJUVANT THERAPY – DISCUSSION (2/2)

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- CheckMate 238 and KEYNOTE 054 (1076O and LBA46) have not shown practice-changing data

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Relapsed/Refractory Metastatic Melanoma

CAROLINE ROBERT, MD, PHD

LBA44: Lenvatinib (len) plus pembrolizumab (pembro) for advanced melanoma (MEL) that progressed on a PD-1 or PD-L1 inhibitor: Initial results of LEAP-004. A.M. Arance Fernandez, et al

EPICS

Background

> Identification of safe and effective treatment options for melanoma that progressed on anti–PD-1 based therapy is a

1081MO: Efficacy of ipilimumab plus nivolumab or ipilimumab plus fotemustine vs fotemustine in patients with melanoma metastatic to the brain: primary analysis of the phase III NIBIT-M2 trial. A.M. Di Giacomo, et al

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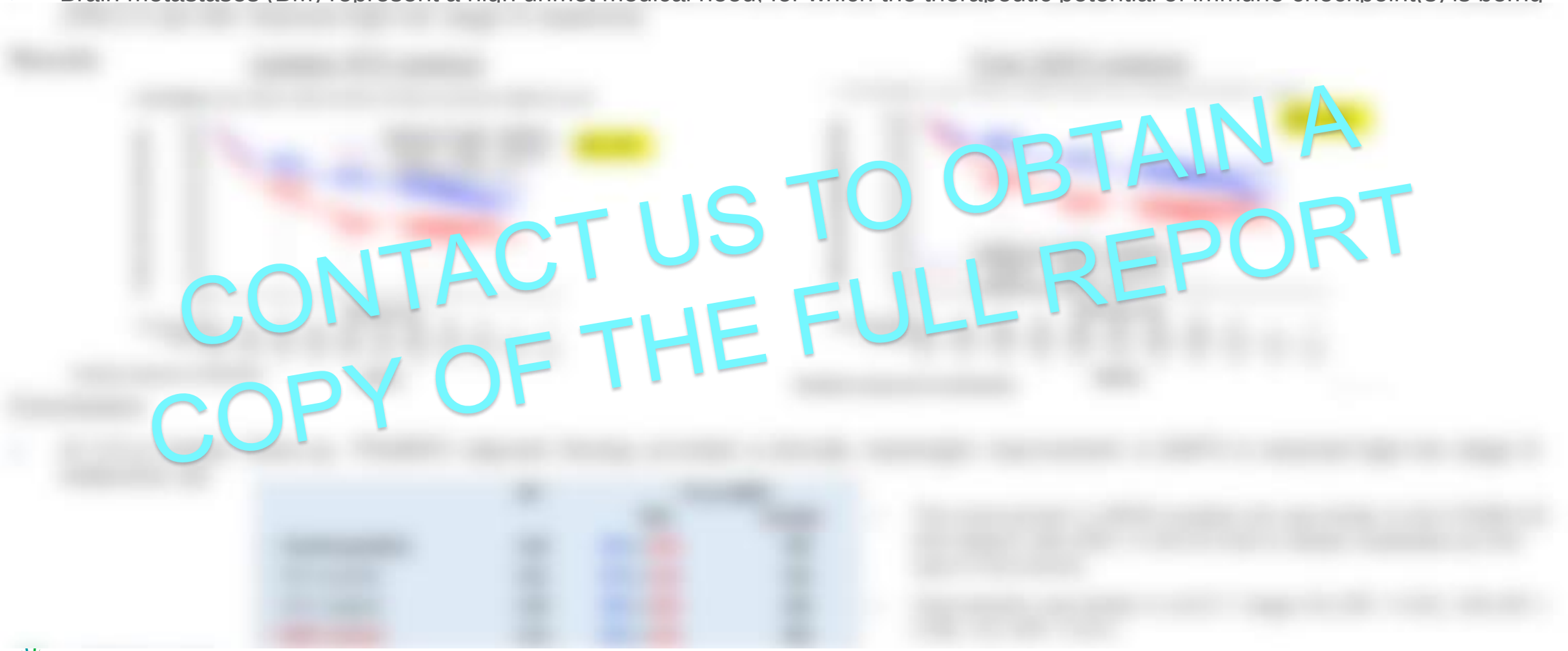
Background

> Brain metastases (BM) represent a high unmet medical need, for which the therapeutic potential of immune checkpoint(s) is being



1083MO: Final Results from ILLUMINATE-204, a Phase 1/2 Trial of Intratumoral Tilsotolimod in Combination with Ipilimumab in PD-1 Inhibitor Refractory Advanced Melanoma. C. Haymaker, et al

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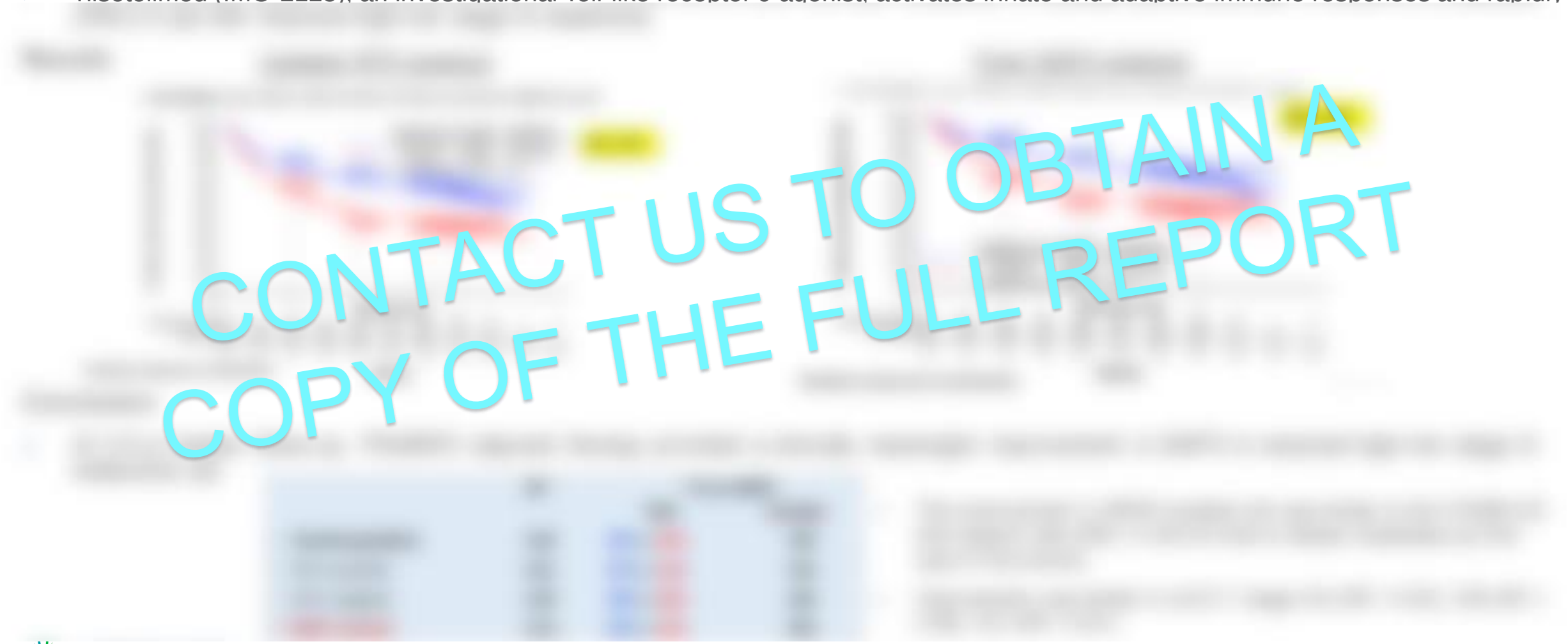
Background

> Tilsotolimod (IMO-2125), an investigational Toll-like receptor 9 agonist, activates innate and adaptive immune responses and rapidly



1080MO: The value of local therapy in treatment of solitary melanoma progression upon immune checkpoint inhibition. J.M. Versluis, et al

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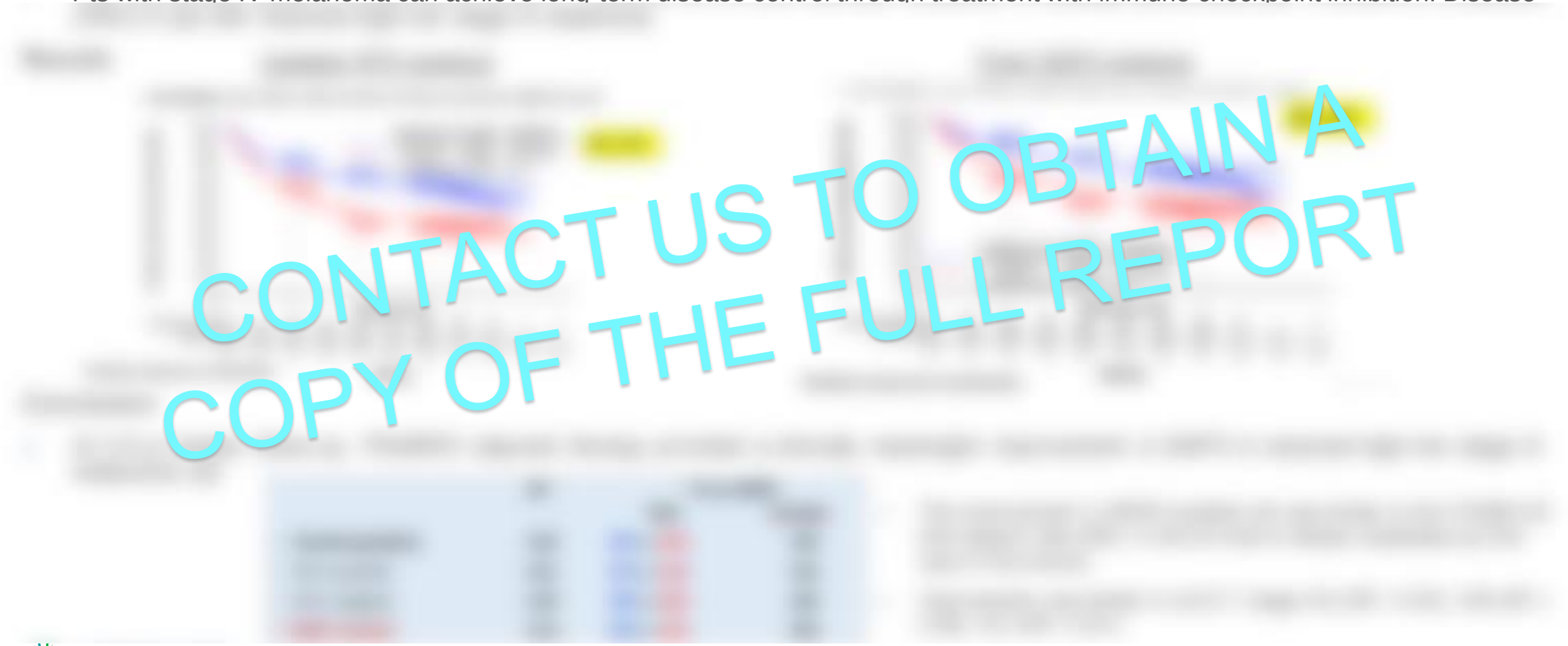
Background

> Pts with stage IV melanoma can achieve long-term disease control through treatment with immune checkpoint inhibition. Disease



1112P: Intralesional therapy with Talimogene Laherparepvec for stage IIIB-IVM1a melanoma is able to achieve a high rate of complete and durable responses and is associated with tumor load. E. Stahlie, et al

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Background

> Talimogene laherparepvec (T-VEC) is a genetically modified herpes simplex type 1 virus and known as an effective oncolytic IO for

RELAPSED/REFRACTORY METASTATIC MELANOMA – DISCUSSION (1/2)

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- Experts reiterated that IPI + NIVO has become the standard of care for relapsed/refractory

RELAPSED/REFRACTORY METASTATIC MELANOMA – DISCUSSION (2/2)

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- T-VEC (real-world cohort analysis; 1112P)

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Immunotherapy for 1L Metastatic Melanoma

REINHARD DUMMER, MD

LBA45: First report of efficacy and safety from the phase II study SECOMBIT (SEquential COMBo Immuno and Targeted therapy study). P. Ascierto, et al

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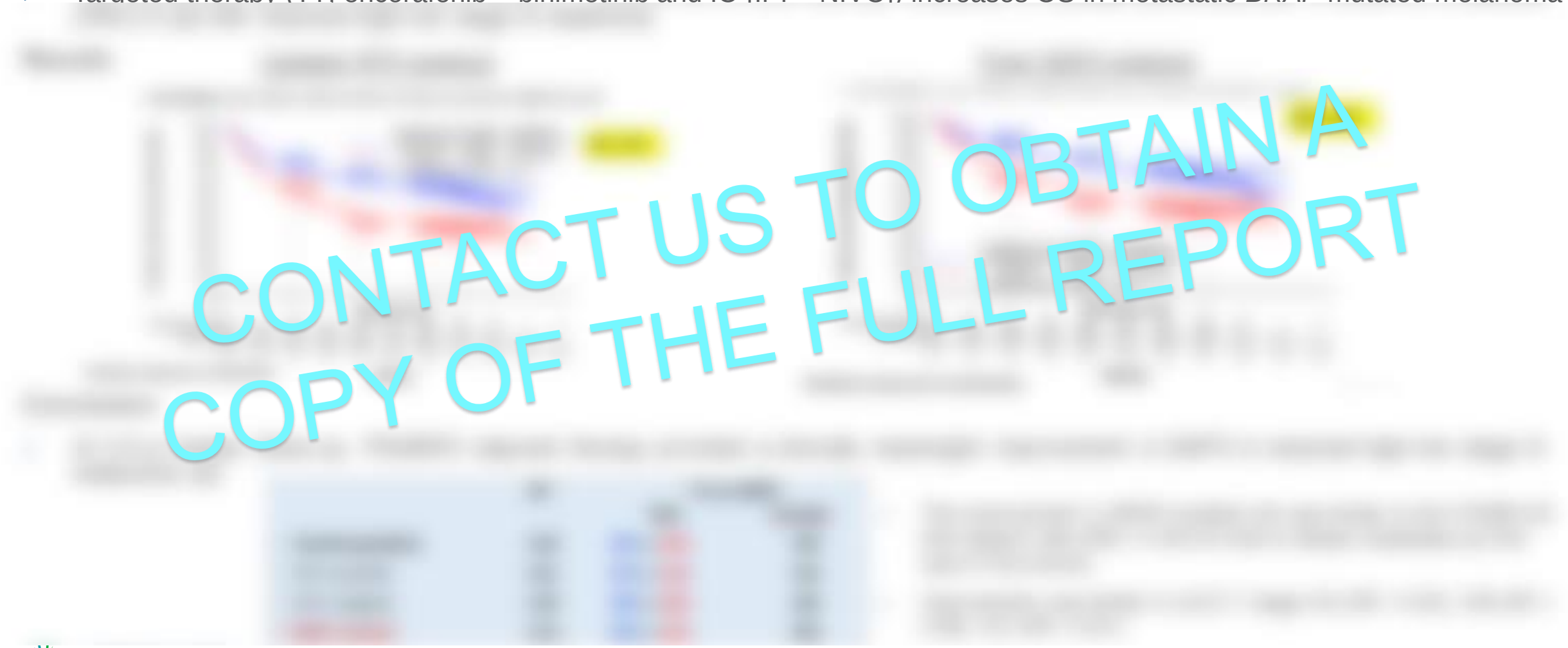
Background

> Targeted therapy (TT; encorafenib + binimetinib and IO [IPI + NIVO]) increases OS in metastatic *BRAF*-mutated melanoma



1082MO: 5-year characterization of complete responses in patients with advanced melanoma who received nivolumab plus ipilimumab (NIVO+IPI) or NIVO alone. C. Robert, et al

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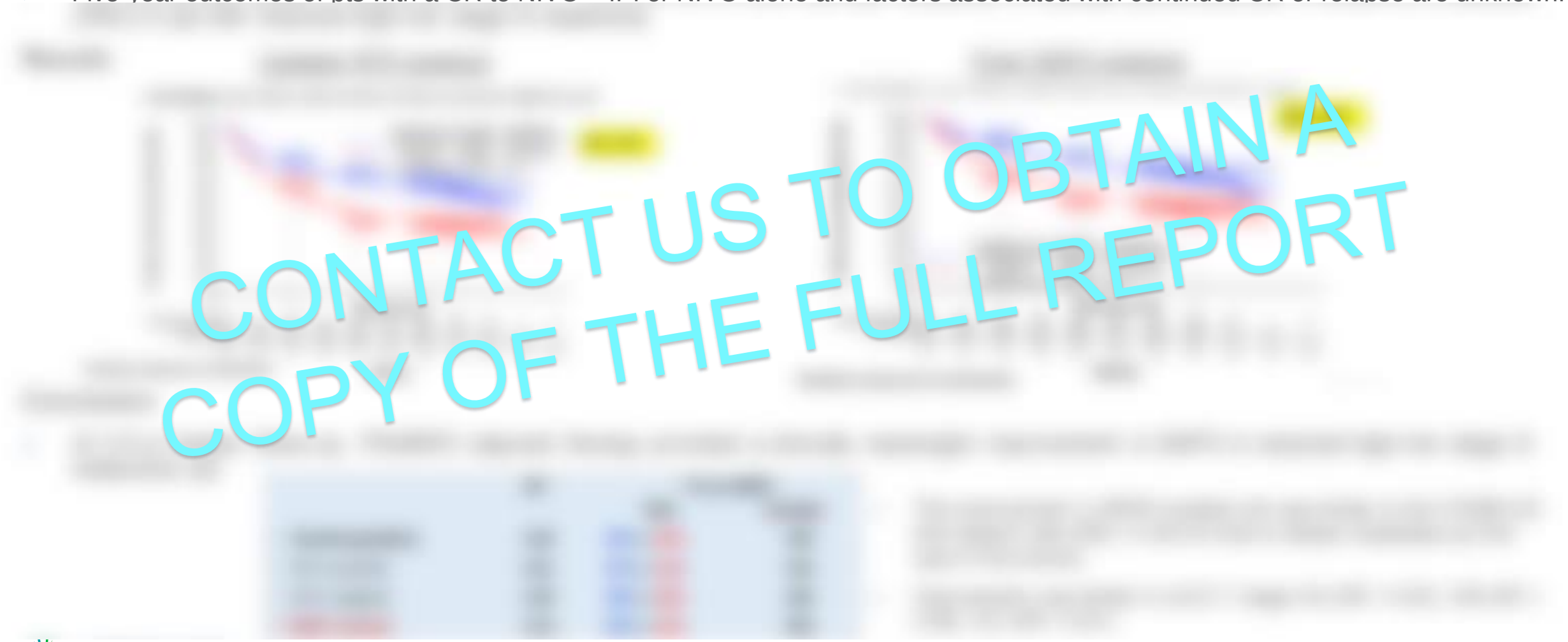
Background

> Five-year outcomes of pts with a CR to NIVO + IPI or NIVO alone and factors associated with continued CR or relapse are unknown.



1139P: Long-Term Safety Profile of Pembrolizumab Monotherapy and Relationship With Clinical Outcome: A Pooled Analysis of Patients With Advanced Melanoma. O. Hamid, et al

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Background

> Long-term safety of PEMBRO in metastatic melanoma was analyzed using data from phase I–III studies: KEYNOTE-001,

1105P: Estimating long-term survivorship in patients with advanced melanoma treated with immune-checkpoint inhibitors: analyses from the phase 3 CheckMate 067 trial. P. Mohr, et al

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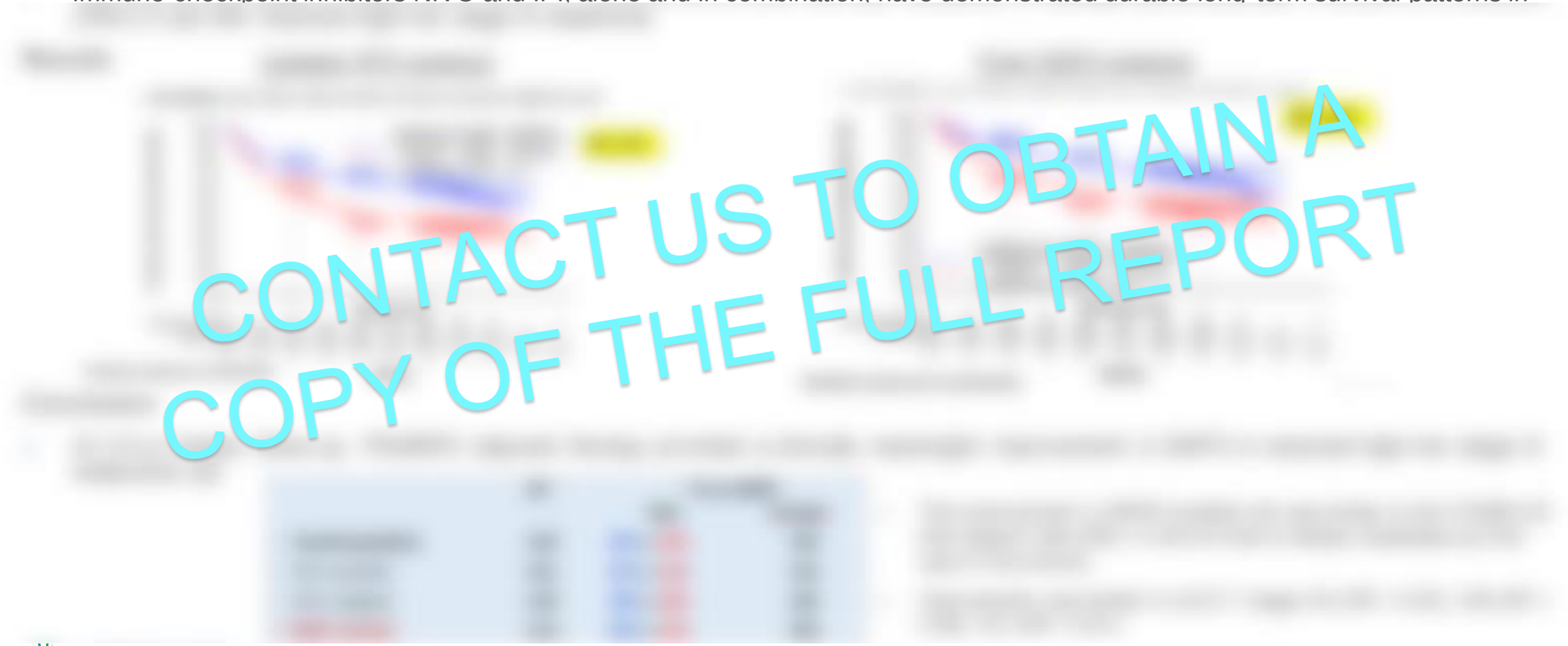
Background

> Immune-checkpoint inhibitors NIVO and IPI, alone and in combination, have demonstrated durable long-term survival patterns in



1147P: Primary Ipilimumab/Nivolumab immunotherapy followed by adjuvant Nivolumab in locally advanced or oligometastatic melanoma: preliminary results. E. Cocorocchio, et al

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Background

> The aim of neoadjuvant therapy in locally advanced or oligometastatic melanoma is to facilitate radical resection, improve outcomes,

IMMUNOTHERAPY FOR 1L METASTATIC MELANOMA – DISCUSSION (1/3)

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- IPI + NIVO remains the standard of care for frontline treatment in the metastatic setting. However

IMMUNOTHERAPY FOR 1L METASTATIC MELANOMA – DISCUSSION (2/3)

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- The pooled analysis of data from the KEYNOTE-001, KEYNOTE-002, and KEYNOTE-006 (1139P)

IMMUNOTHERAPY FOR 1L METASTATIC MELANOMA – DISCUSSION (3/3)

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- Neoadjuvant treatment with IPI + NIVO before surgical resection in locally advanced or

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1L *BRAF*-Mutated Metastatic Melanoma – Long-term Results and Strategies to Improve on MAPK-Targeted Therapies

JAMES LARKIN, MD, PHD

LBA43: Spartalizumab plus dabrafenib and trametinib (Sparta-DabTram) in patients (pts) with previously untreated BRAF V600–mutant unresectable or metastatic melanoma: Results from the randomized part 3 of the phase III COMBI-i trial. P. Nathan, et al

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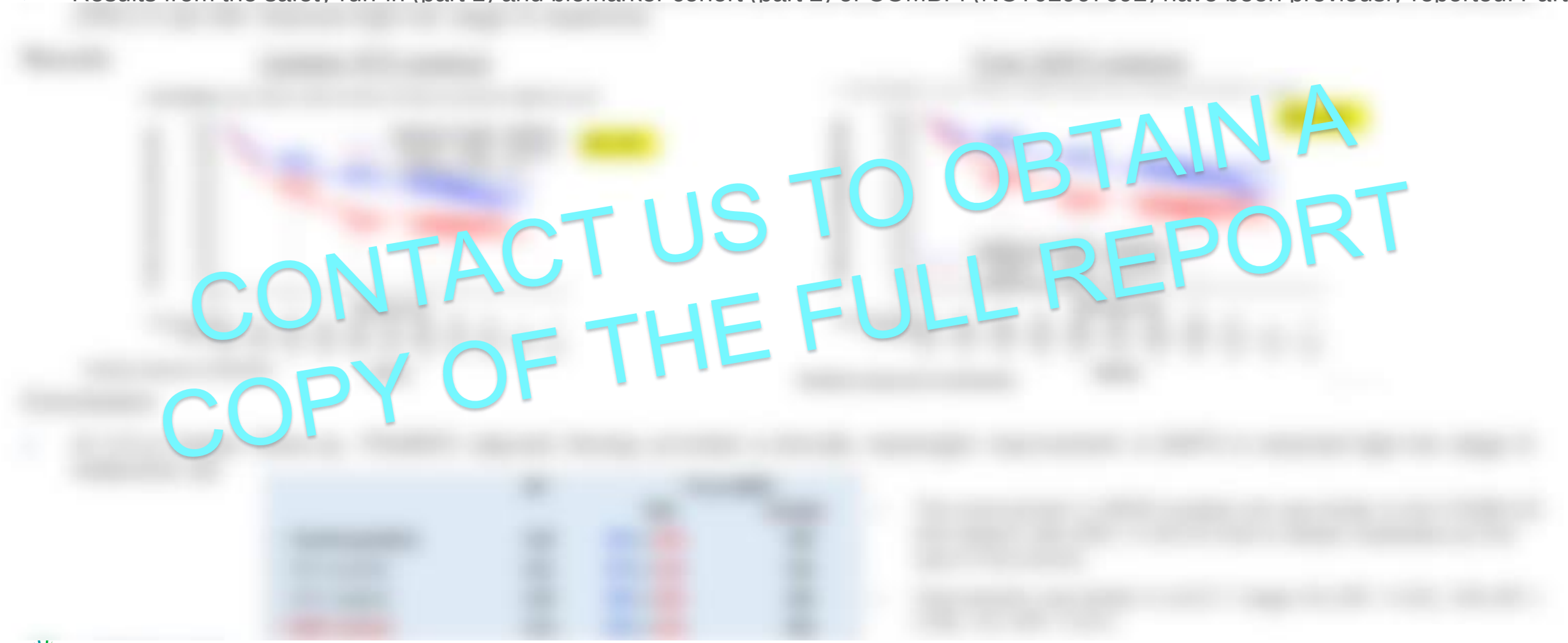
Background

> Results from the safety run-in (part 1) and biomarker cohort (part 2) of COMBI-i (NCT02967692) have been previously reported. Part



1137P: Incidence and time course of adverse events (AEs) with atezolizumab (A) in combination with vemurafenib (V) and cobimetinib (C) in the phase 3 IMspire150 study. K. Lewis, et al

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Background

1098P: Neoadjuvant cytoreductive treatment with BRAF/MEK inhibition of prior unresectable regionally advanced melanoma to allow complete surgical resection, REDUCTOR: a prospective single arm phase II trial. M. Rohaan, et al

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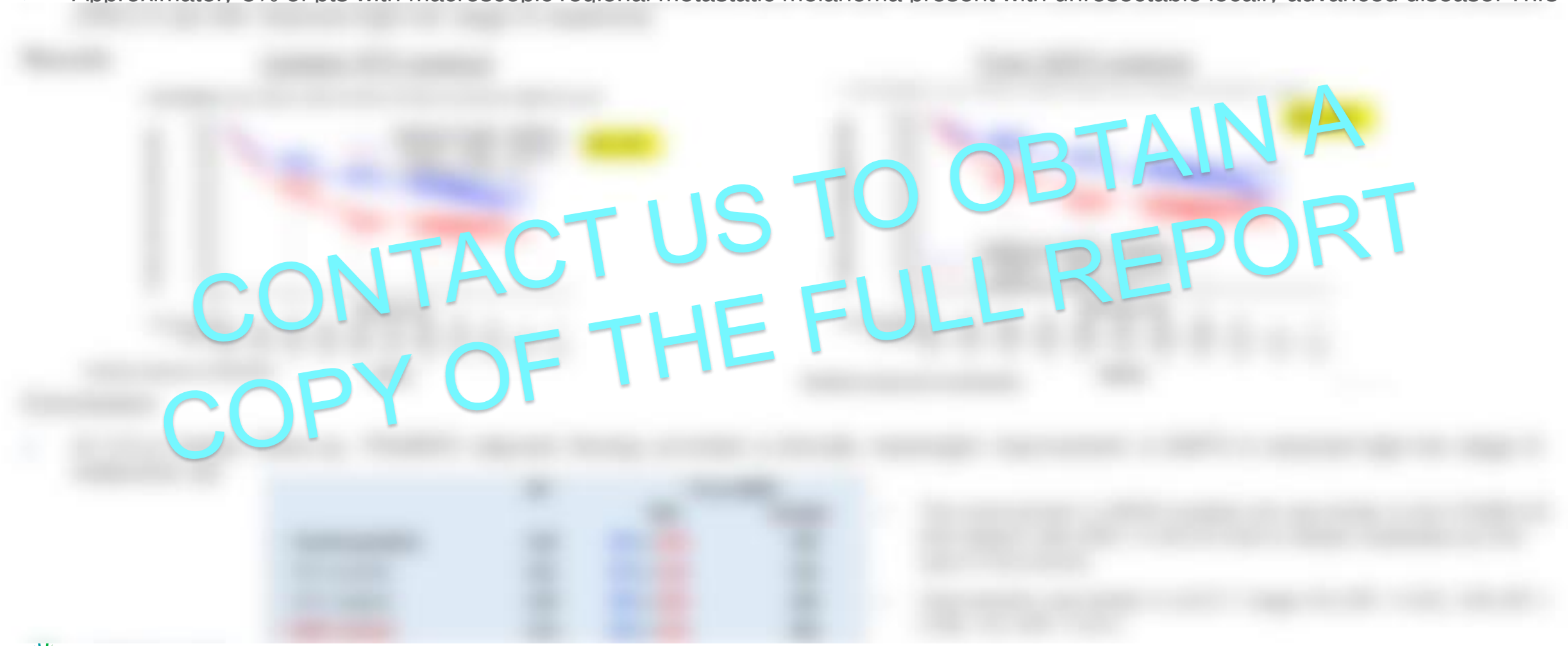
Background

> Approximately 5% of pts with macroscopic regional metastatic melanoma present with unresectable locally advanced disease. This



1108P: Real World (RW) Sequencing Outcomes with Immunotherapy and Targeted Therapy (TT) in BRAF+ Metastatic Melanoma (The NOBLE Study Series). A. Betof Warner, et al

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Background

1L *BRAF*-MUTATED METASTATIC MELANOMA – DISCUSSION (1/2)

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- COMBI-i trial (LBA43)

1L *BRAF*-MUTATED METASTATIC MELANOMA – DISCUSSION (2/2)

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- REDUCTOR trial (1098P)