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ONCOS-102 in mesothelioma

Dr Magnus Jaderberg
Chief Medical Officer
Targovax

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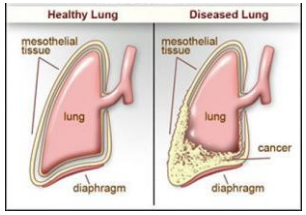
ONCOS

CLINICAL DEVELOPMENT STRATEGY

1

Path-to-market
Mesothelioma

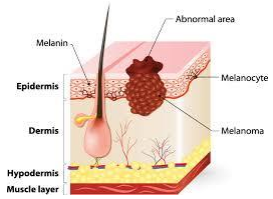


Target launch indication

- Ongoing Phase I/II

2

Proof-of-concept
CPI refractory

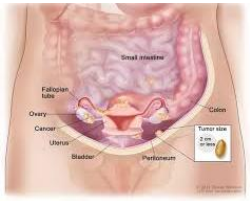


Indications with no/ limited effect of CPIs

- Ongoing melanoma Phase I

3

Proof-of-concept
New CPI indication

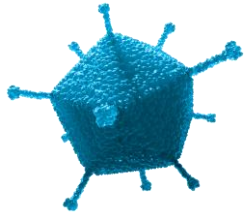


Peritoneal malignancies

- Ongoing Phase I/II in ovarian and colorectal

4

Next generation
oncolytic viruses



Targeting new indications

- Novel targets and mode-of-action

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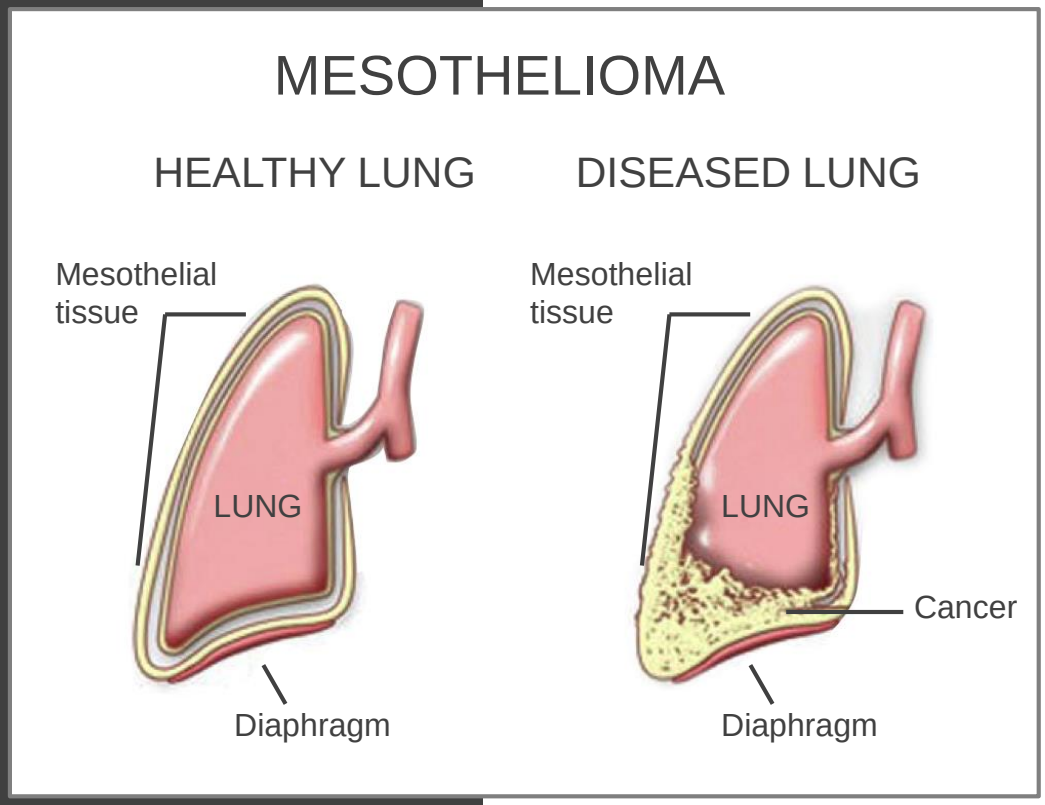
ONCOS-102 target launch indication

MALIGNANT PLEURAL MESOTHELIOMA

- **Orphan disease**, estimated 15,000 new cases per year (EU, USA, Australia)
- **Incidence is increasing** worldwide and is predicted to peak in 5-10 years
- Often **caused by asbestos** exposure, with a latency period of up to 40 years before diagnosis
- Aggressive cancer form with **median survival of 12 months**
- **No significant treatment advance** in the last decade



MESOTHELIOMA IS SHORTEST PATH-TO-MARKET

Rationale for ONCOS-102 opportunity in mesothelioma:

Become frontline therapy

- **Phase I results** indicate potential of ONCOS-102 in mesothelioma
- **Ongoing randomized phase I/II trial** combining ONCOS-102 with SoC chemotherapy
- **Good safety profile**

Orphan Drug Designation

- High unmet medical need, ONCOS-102 has **orphan drug designation**
- Opportunity for priority regulatory review, and **quick route-to-market**
- 7 year **market exclusivity** in the US and 10 years in the EU

Limited competition

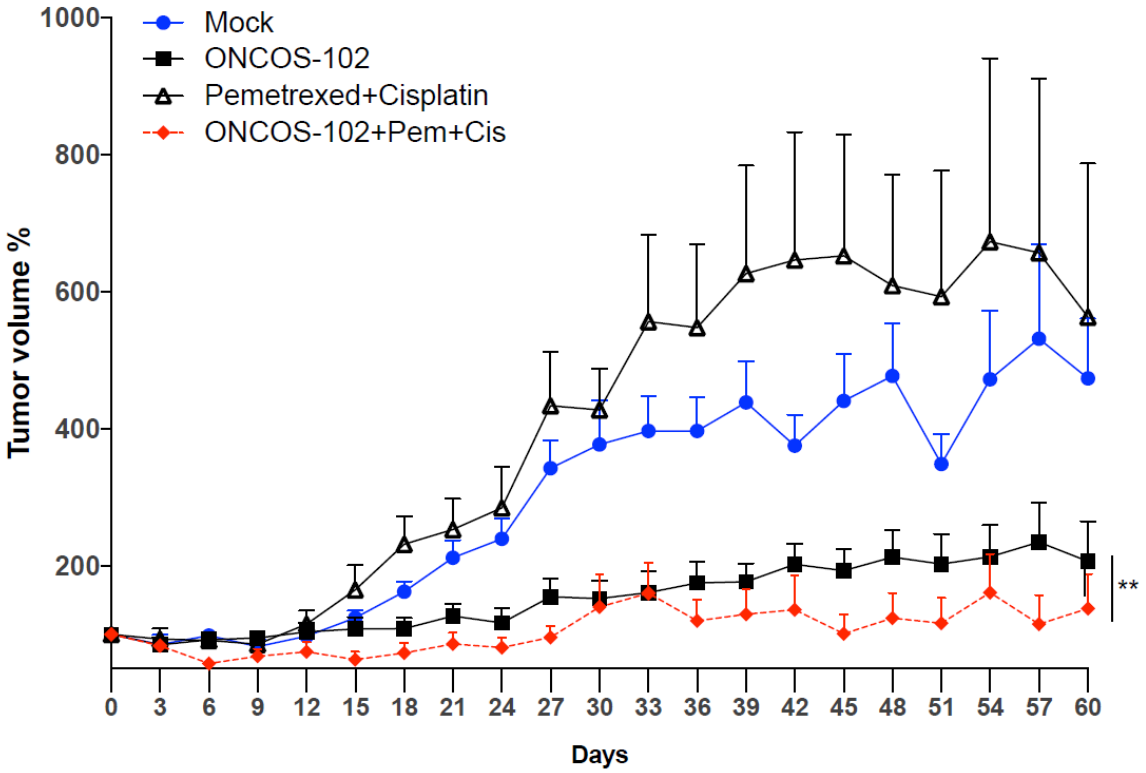
- CPIs show some early signs of efficacy, but are **potential ONCOS-102 combinations**, rather than competitors
- **No competing viruses** and few vaccines in current clinical development in mesothelioma

SYNERGY BETWEEN ONCOS-102 AND CHEMOTHERAPY

mesothelioma mouse model

Anticancer effect of ONCOS-102 and standard of care chemotherapy in xenograft mouse mesothelioma model

% change in tumor volume, 7 animals per group (14 tumors/group)



Effects observed at Day 60:

ONCOS vs. mock

56% tumor volume reduction
p < 0.01

ONCOS vs. pem/cis

63% tumor volume reduction
p < 0.01

ONCOS+pem/cis vs. pem/cis

75% tumor volume reduction
p < 0.001

ONCOS+pem/cis vs ONCOS

33% tumor volume reduction p < 0.01

SOURCE: Kuryk et al., Int J Cancer, 10 June 2016

ONCOS-102 CAN TURN MESOTHELIOMA LESIONS HOT

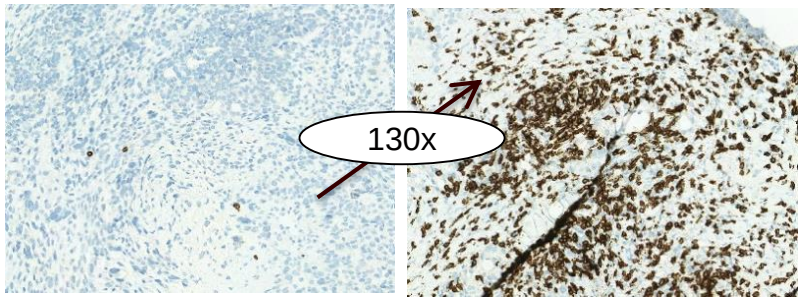
Phase I

CD8+ T-cells in tumor
Tumor biopsy staining

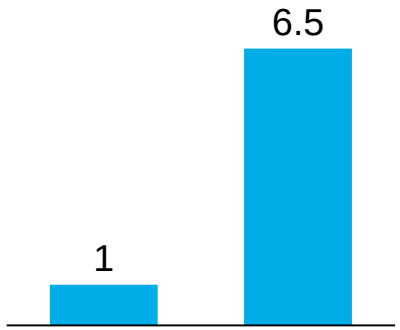
CD4+ T-cells in tumor
Fold change

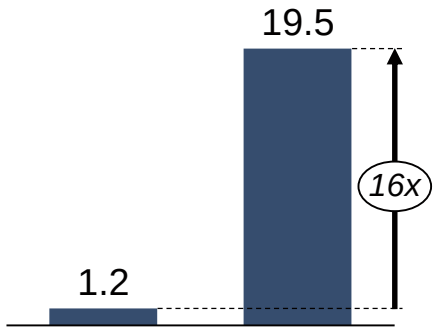
PD-L1 positive tumor cells
% of total

Mesothelioma *– Phase I, patient 14*

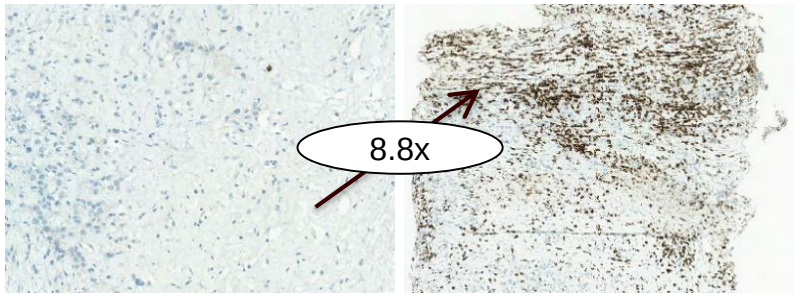


Baseline Week 5

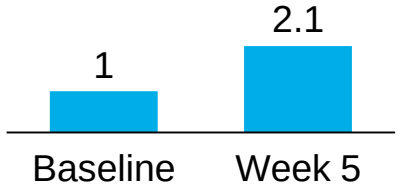


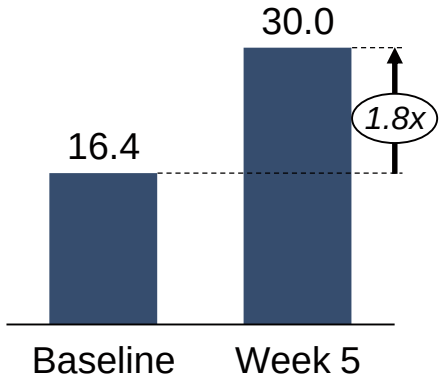


Mesothelioma *– Phase I, patient 9*



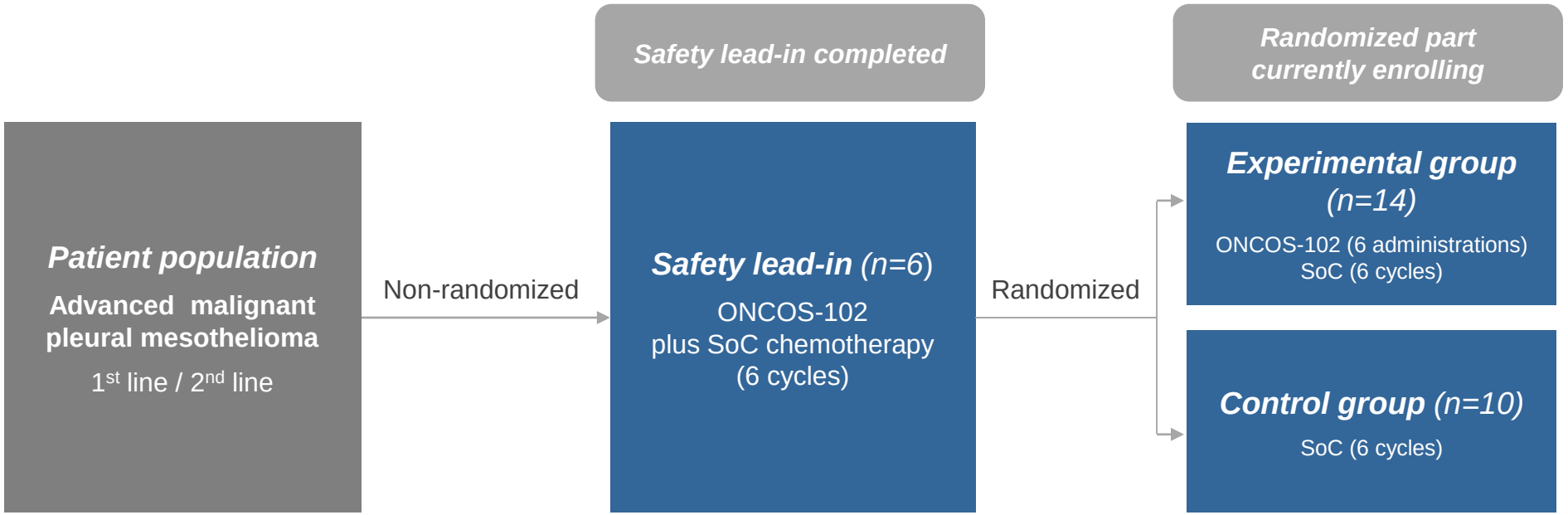
Baseline Week 5





Ranki et al., Journal for Immunotherapy of Cancer 2016, 4(17)

PHASE I/II STUDY DESIGN IN COMBINATION WITH SoC



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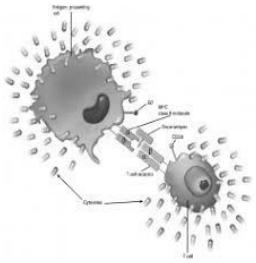
SIGNAL OF EFFICACY IN THE FIRST 6 PATIENTS

1
Safety

- ✓ ONCOS-102 **well-tolerated** in combination **with chemotherapy**

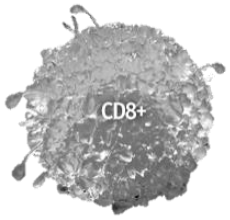
2
Innate immune activation

- ✓ **Systemic increase of pro-inflammatory cytokines** in 6/6 patients (IL-6, TNFα and IFNγ)



3
Adaptive immune activation

- ✓ Increase in **tumor infiltration of CD4+ and CD8+ T-cells** in 3/4 patients



4
Clinical benefit

- ✓ **Signal of clinical benefit** seen in **3/6 patients** after 6 months
- ✓ **50% disease control rate**

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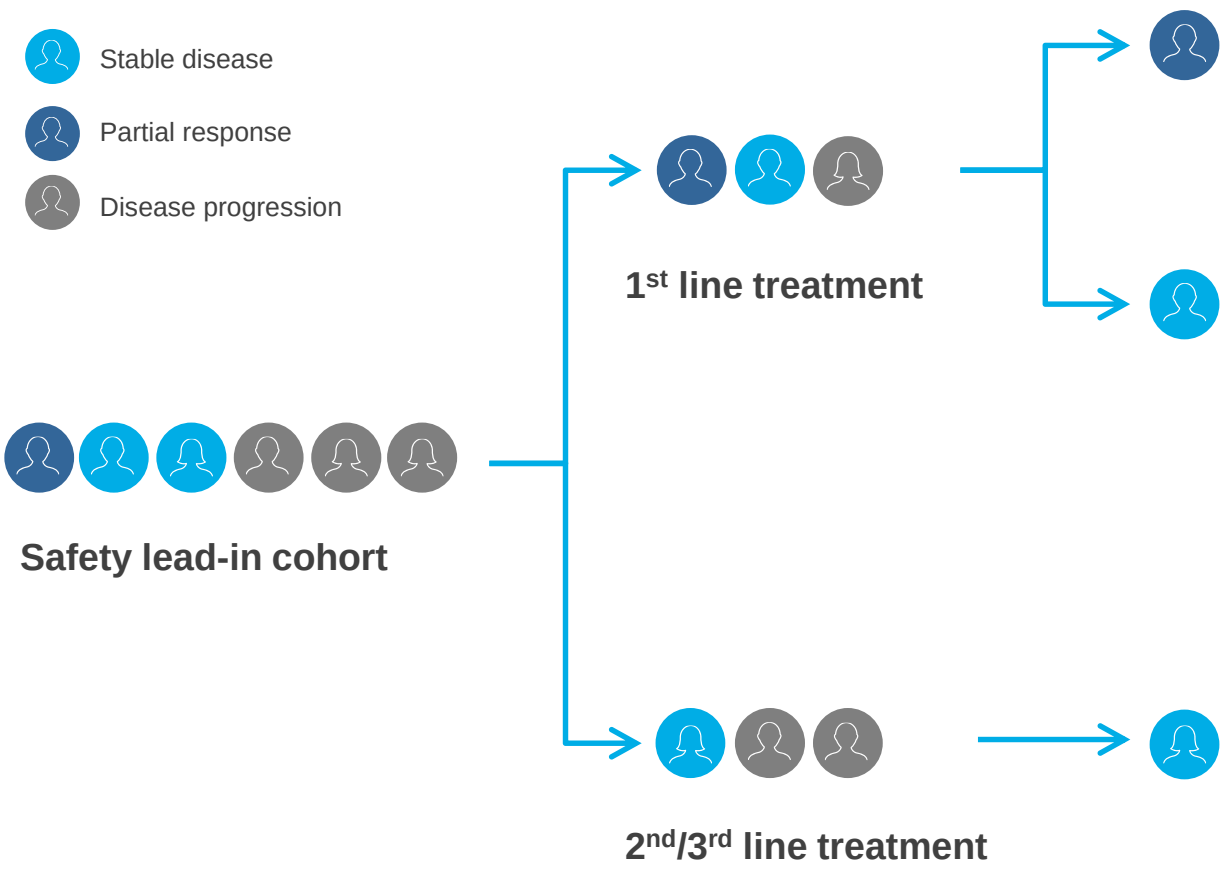
CLINICAL RESPONSES IN SAFETY COHORT



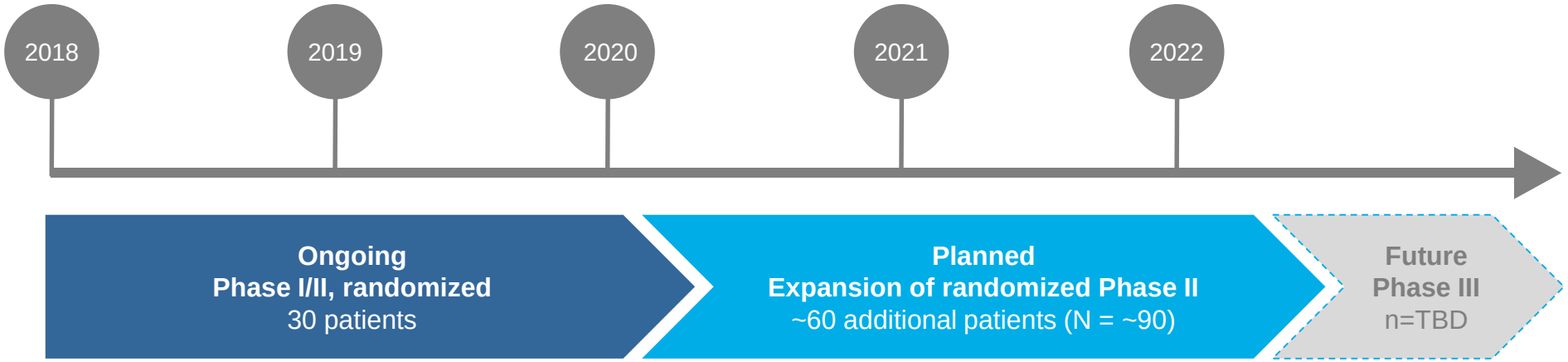
- 50% tumor reduction (CT)
- Partial metabolic response (PET)

- Stabilized tumor (CT)
- No metabolic change (PET)

- Previously progressed on pem/cis in 1st line
- Stabilized tumor (CT)
- Partial metabolic response (PET)
- 50x increase in CD8+
- MAGE-A1 activated CD8+
- 13x increase in CD4+

ONCOS-102 in malignant pleural mesothelioma

DEVELOPMENT STRATEGY AND INDICATIVE TIMELINES



- Randomized ORR and OS data 30 patients
- Decide on possible CPI combination arm
- EMA & FDA advisory meetings

- Randomized ORR and OS data 90 patients
- Potentially use as basis for a submission for conditional approval
- Start Phase III OS trial for full MAA

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