

GSK VACCINES: BUILDING A THERAPEUTIC PORTFOLIO

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Immunotherapy in action

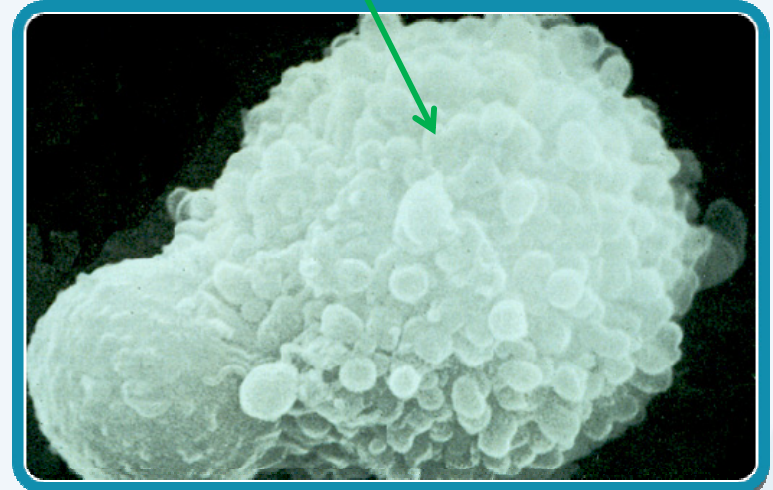
Cytolytic T Lymphocyte (CTL)

Tumour cell



± 20 min
(*in vitro*)

Killed ("lysed")
tumour cell



Antigen-Specific Cancer Immunotherapeutics (ASCI): MAGE-A3

- **Genuine target: identified via screening with anti-tumour killer T-cells**
- **Genuinely tumour-specific: not expressed in normal cells**

- **Easy to detect in patients (RT-PCR on tumour tissue)**
- **Present in major tumour types**
 - Lung 35-50%
 - Bladder 30-58%
 - Liver 24-78%
 - Melanoma 65%
- **Present in early and advanced stages of a given disease**

- **Potentially associated with poor survival prognosis**

Lung cancer and melanoma: need for improved therapies

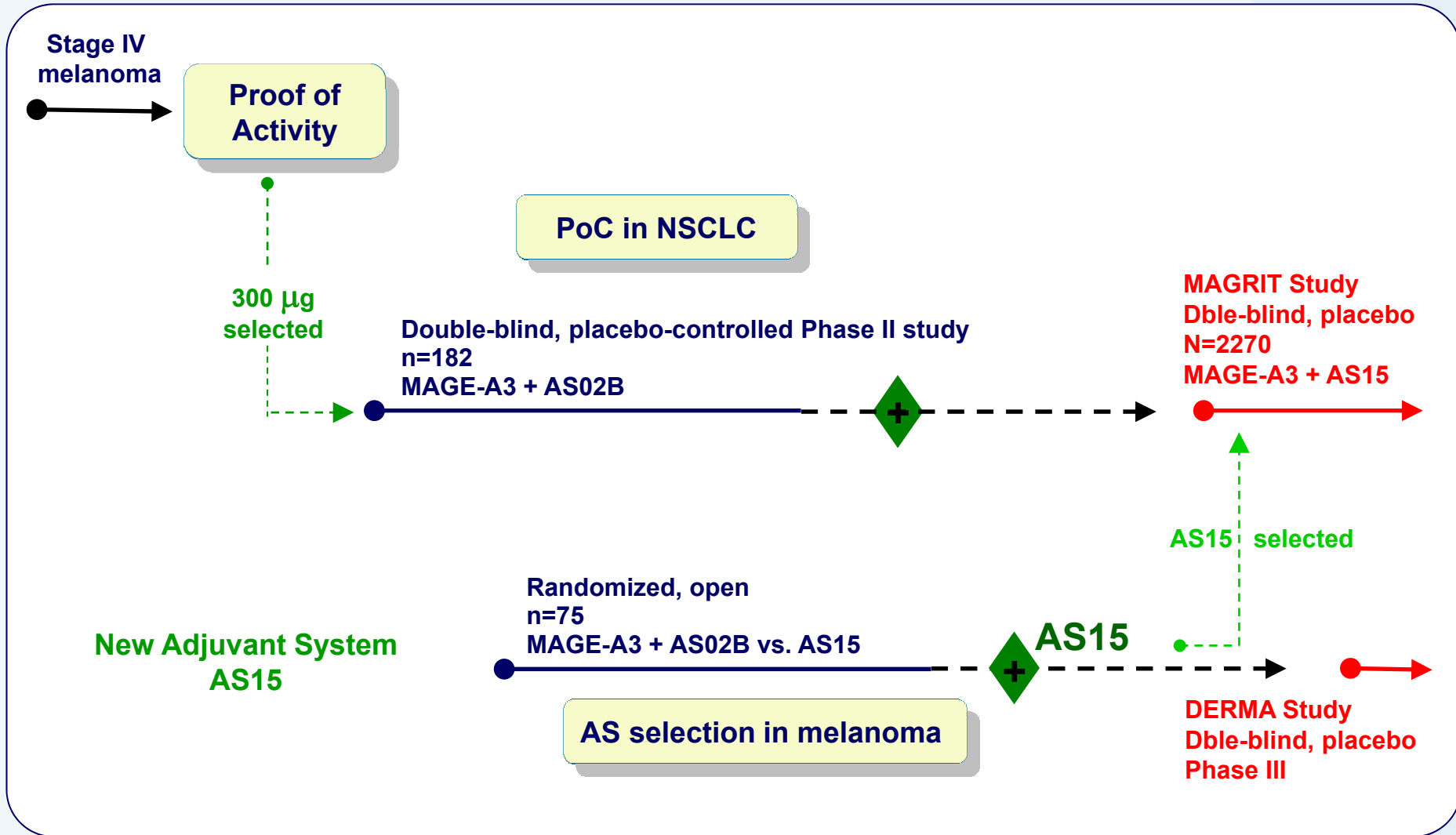
Lung cancer: leading cause of cancer death

- More than 1.3 million new cases a year worldwide
- NSCLC \approx 85% of lung cancer
- More than 1.1 million deaths a year worldwide
- Expected 5-year survival of only 15%
- Current treatments: surgery, chemotherapy, radiotherapy, targeted therapies
 - No real improvement in 5-year survival over last 35 years

Melanoma: most deadly skin cancer

- Approximately 160,000 new cases a year
- Approximately 44,000 deaths a year
- Less than 5% of patients with metastatic disease live beyond 5 years
- Current treatments: surgery, chemotherapy, radiotherapy, immunotherapy
 - No real impact on patient survival so far

MAGE-A3 clinical development programme



MAGE-A3 proof of concept: NSCLC phase II data

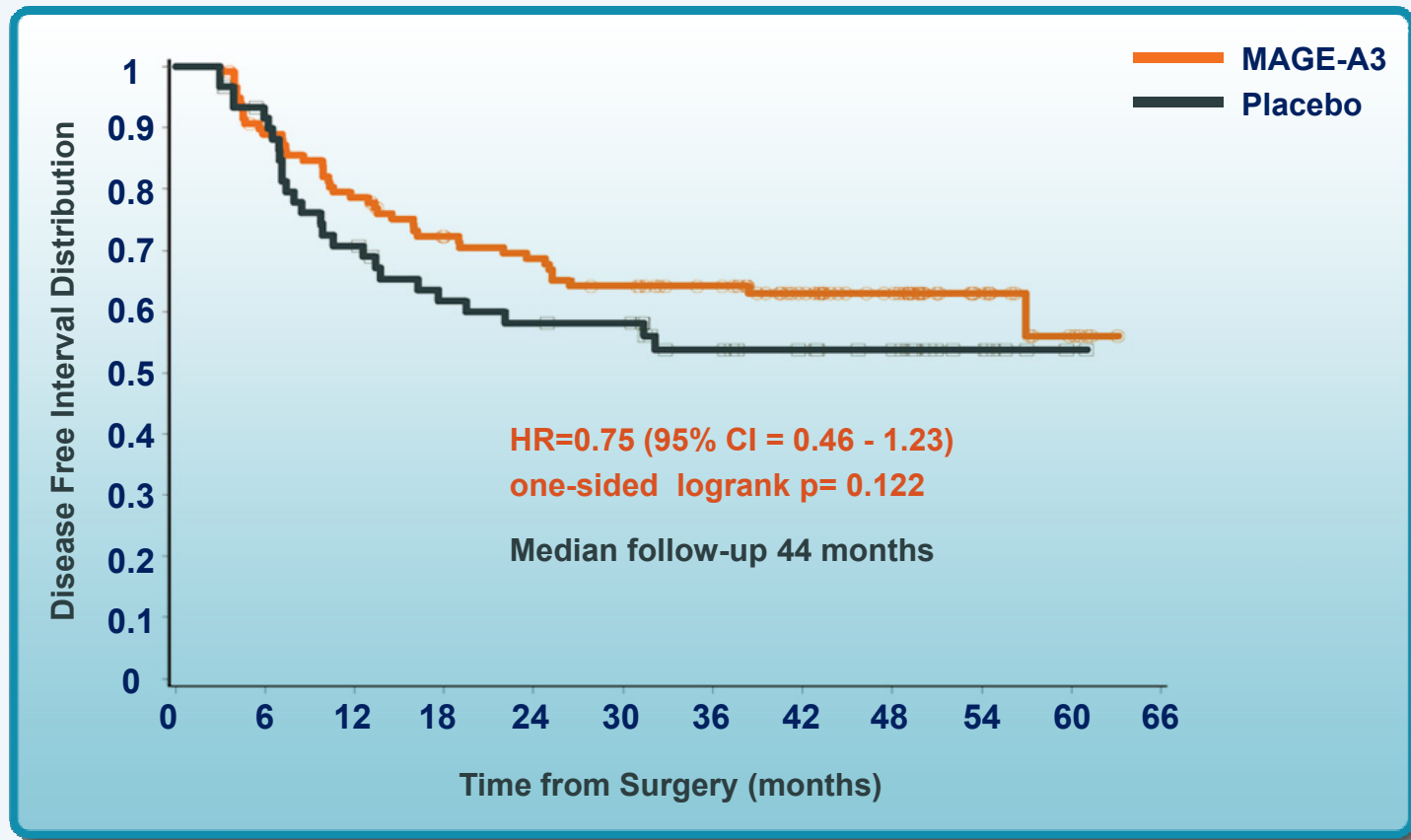
NSCLC

Adjuvant setting – stage IB-II
After surgery – no chemo

Double blind,
placebo controlled phase II
2:1 MAGE-A3/AS02B:placebo

DFS and Survival

180 patients randomized
Interim end 2005



MAGE-A3 proof of concept: melanoma phase II data

Melanoma

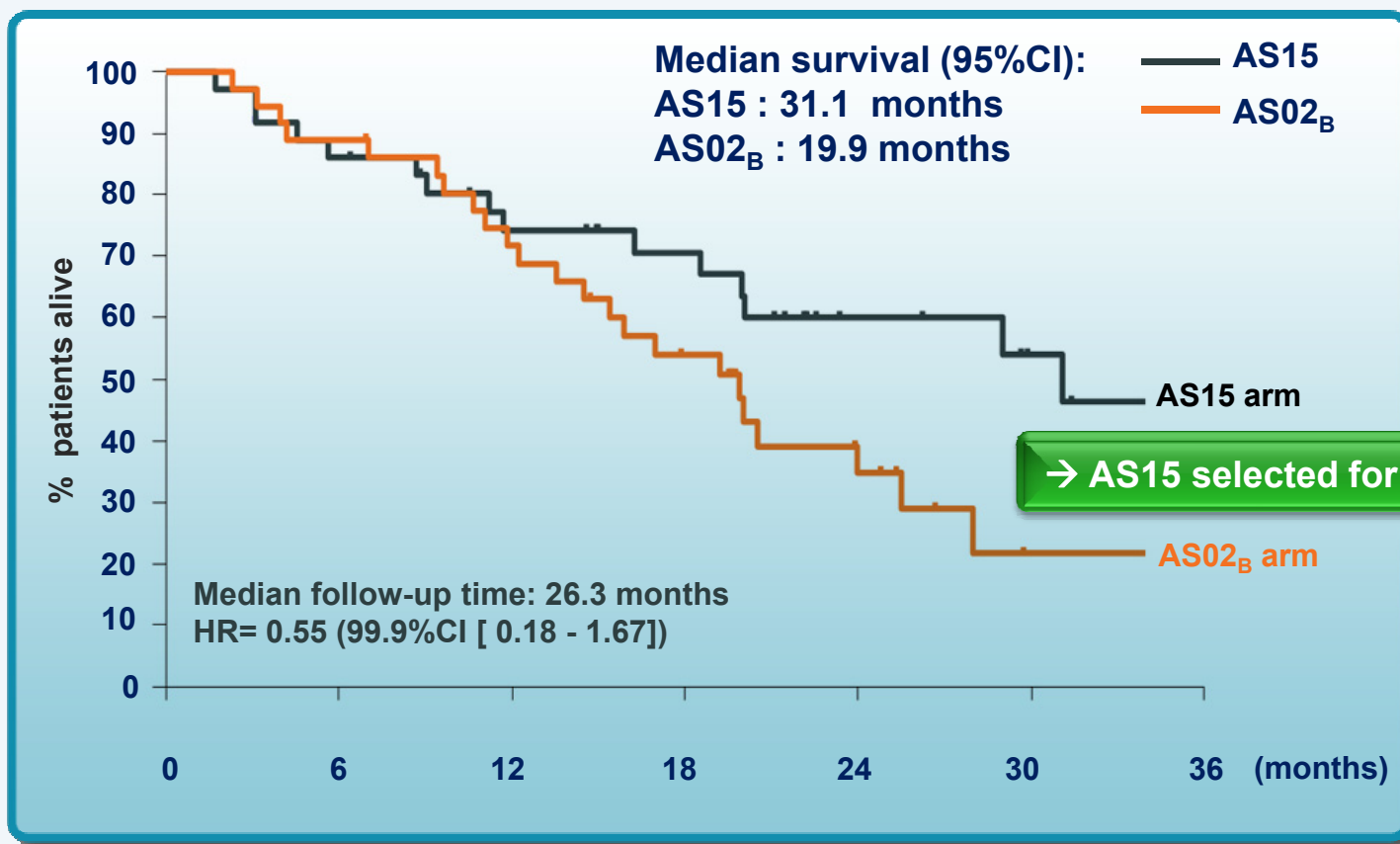
Metastatic setting – stage III-IVa
Progressive

Randomized phase II

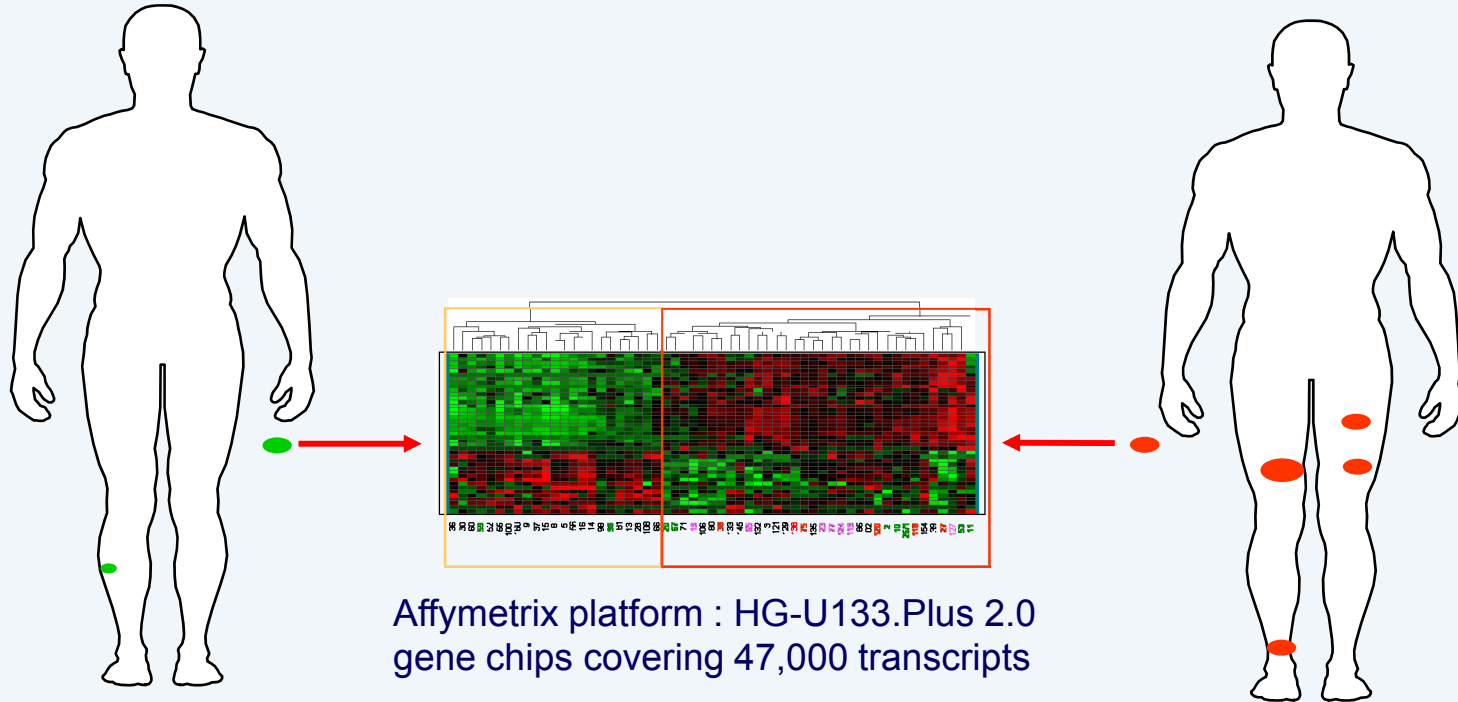
1:1 MAGE-A3 AS02B vs AS15

Tumour response / Surv.

68 patients randomized
Results 2006-2009



Genetic signature predictive of clinical response

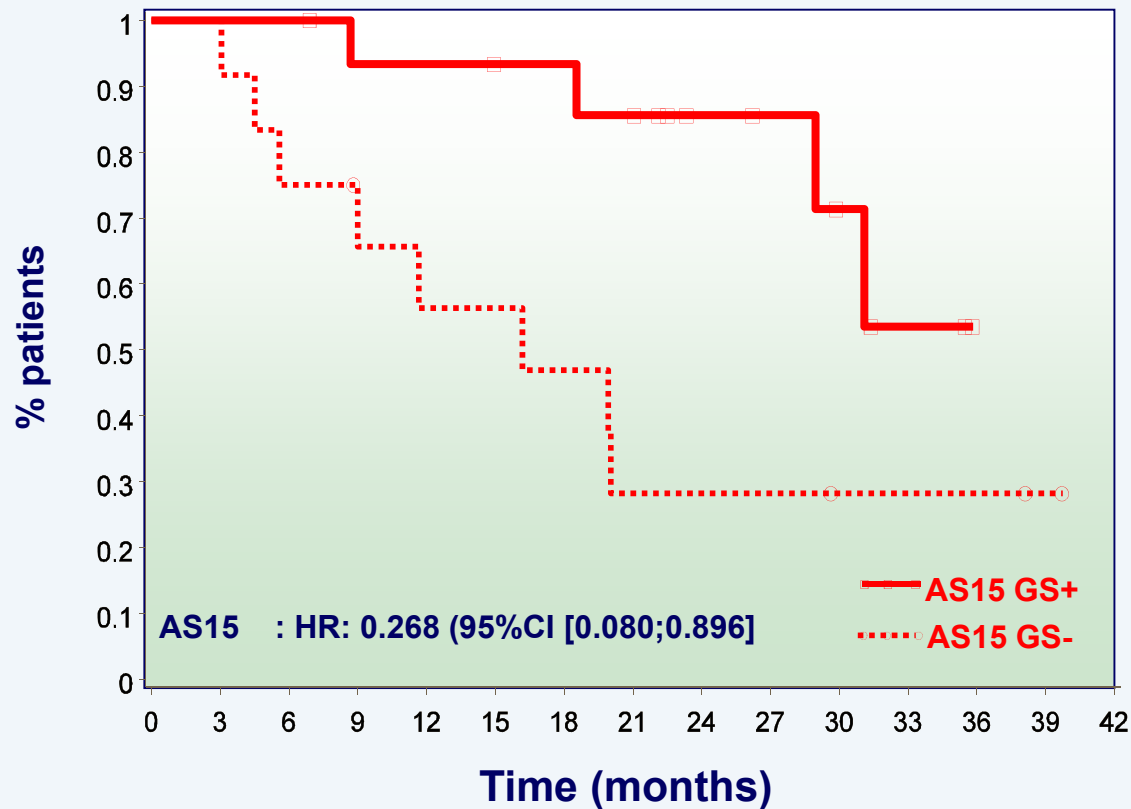


**Clinical benefit
(Responders)**

**Progressive disease
(Non-Responders)**

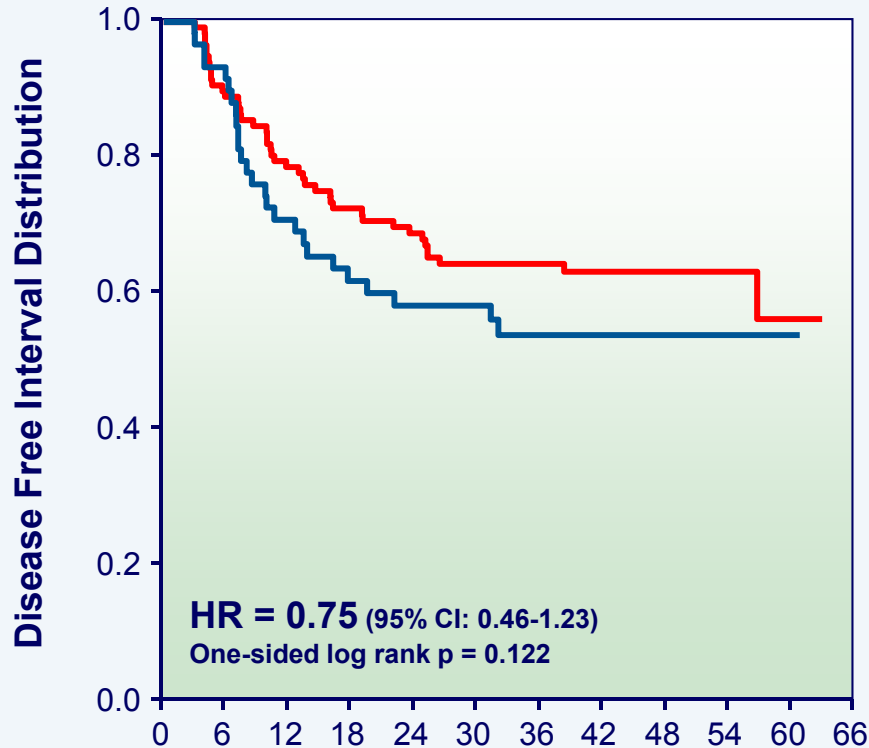
Predictive signature: benefit in melanoma

Gene signature positive



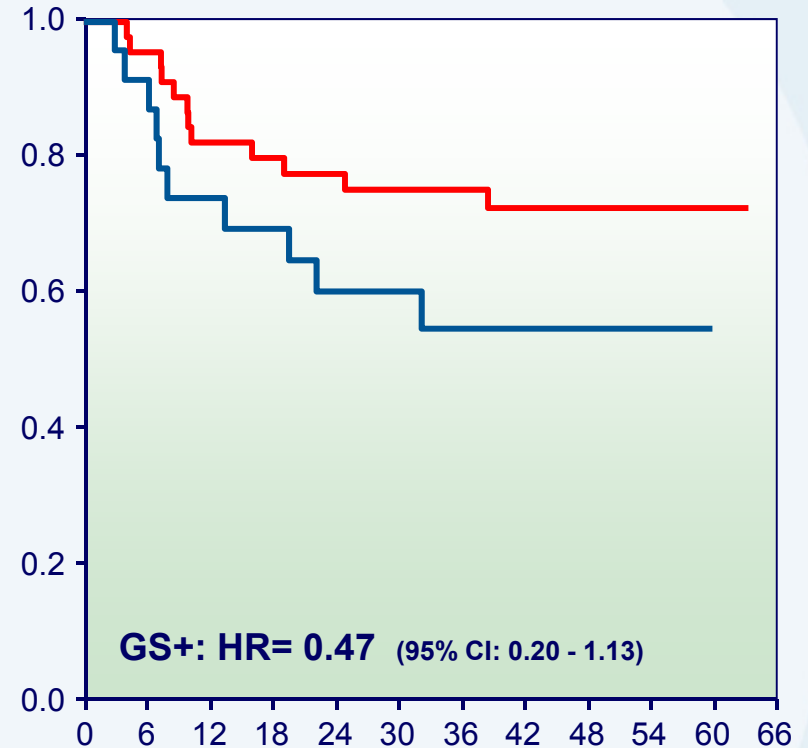
Predictive signature: benefit in NSCLC

Overall study population



Time from surgery (months)

Gene signature positive

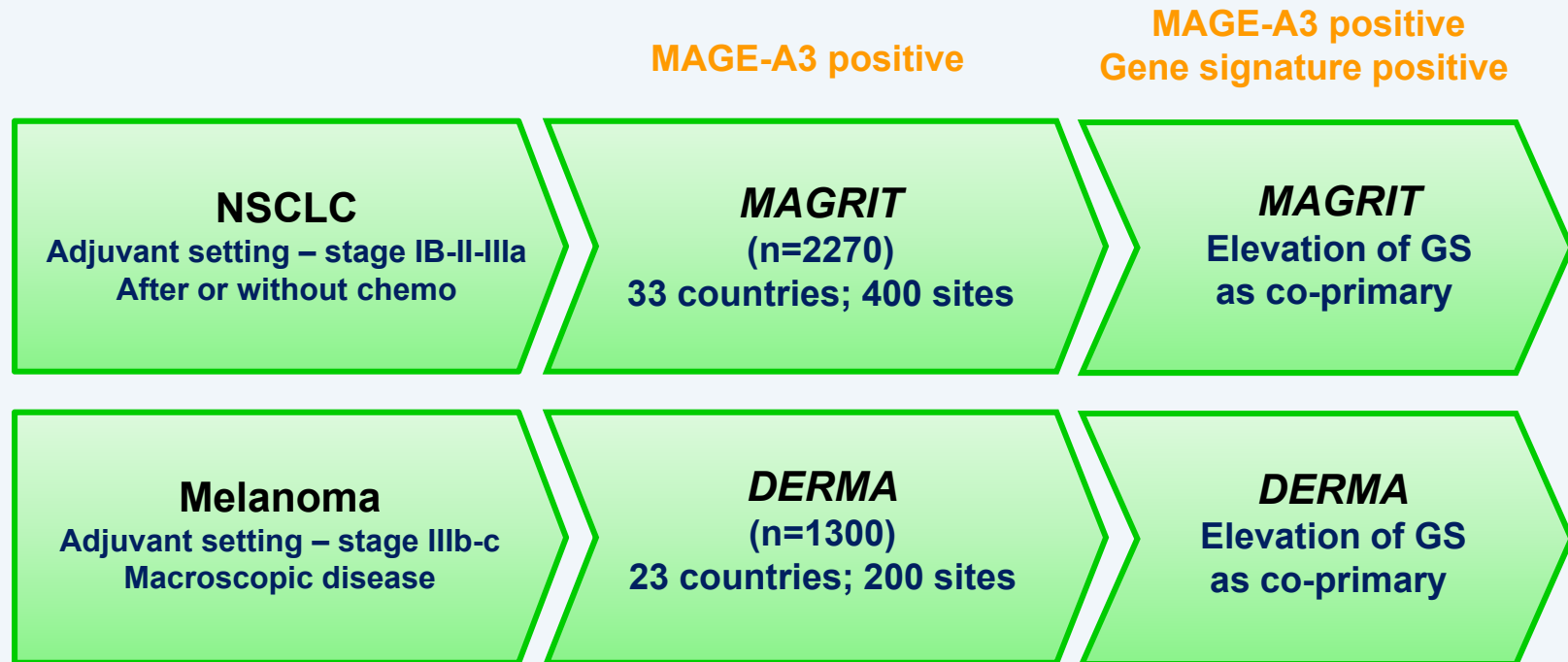


Time from surgery (months)

— MAGE-A3

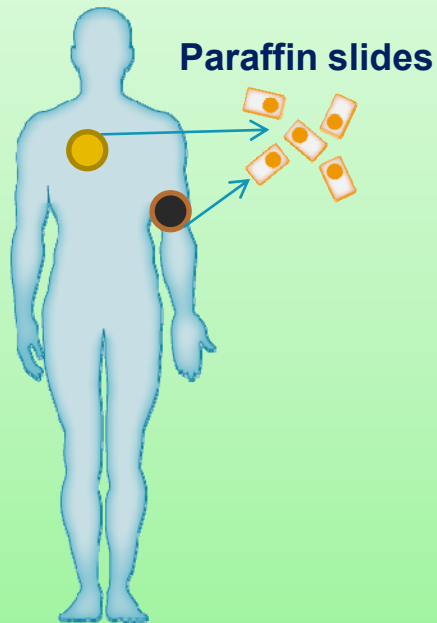
— Placebo

MAGE-A3 phase III: MAGRIT & DERMA



597 randomized
(June 2010)

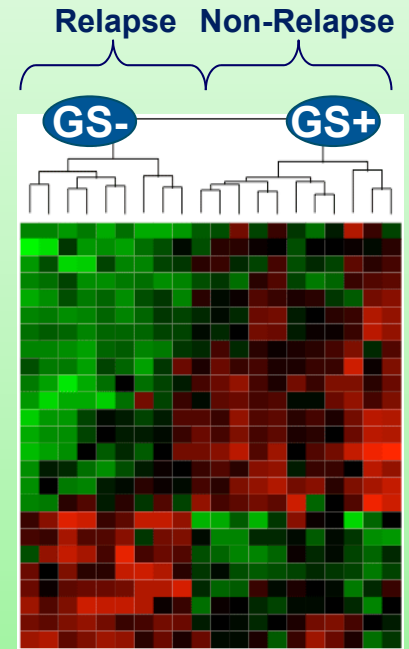
ASCI: diagnostic strategy



- Pre-treatment tumour sample



- MAGE-A3 expression above threshold
- Q-PCR based

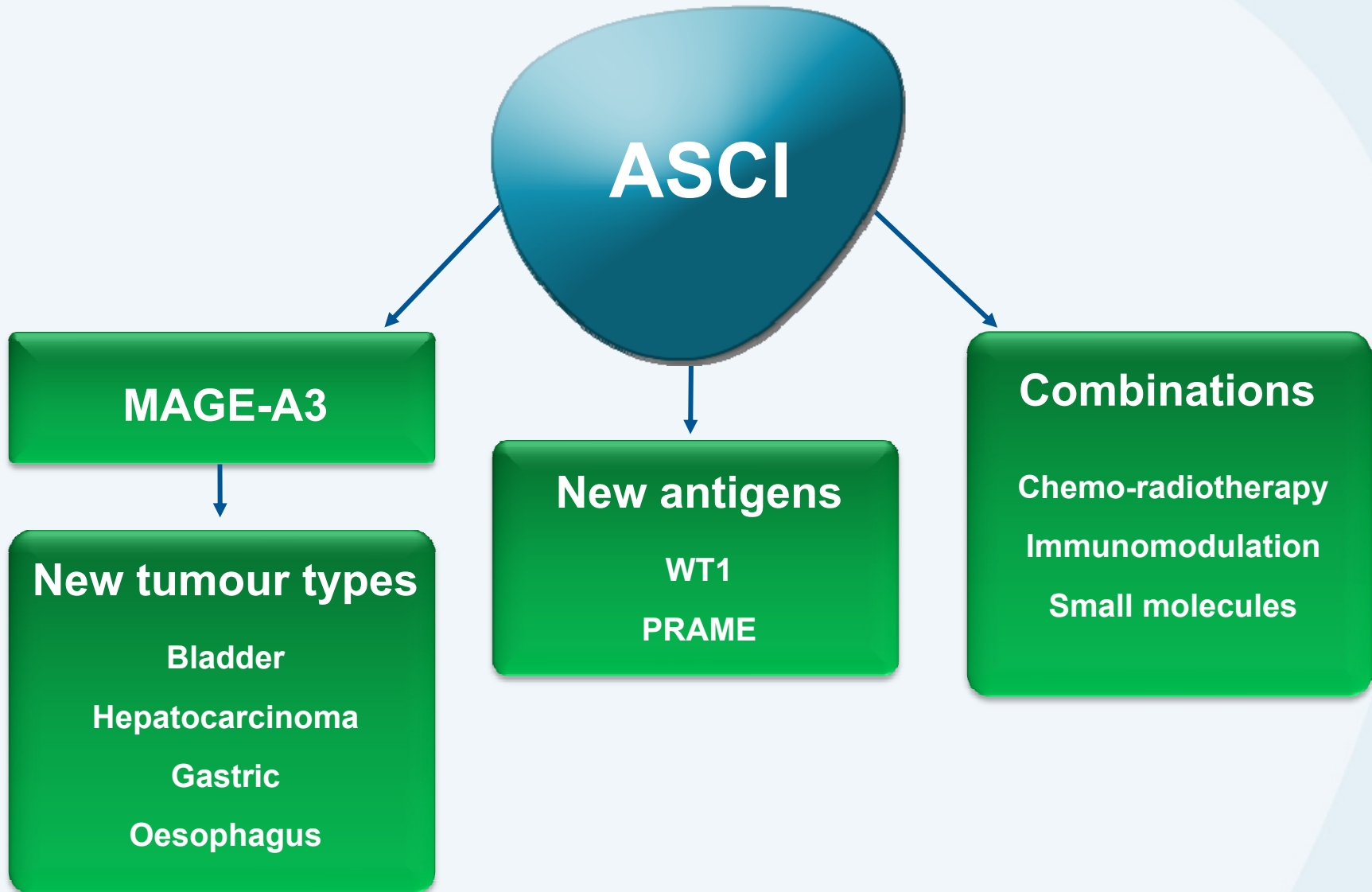


- Presence of an expression pattern
- Multi Q-PCR based

Collaboration with Abbott on MAGE-A3 diagnostic

- Automated molecular diagnostic test
- Based on polymerase chain reaction (PCR) technology
- Using the Abbott m2000™ automated molecular instrument system
- NSCLC deal announced July 2009
- Melanoma deal announced March 2010

Expanding the ASCI portfolio



Alzheimer's disease overview

Alzheimer's disease

- **Most common cause of dementia**
 - Incidence predicted to double by 2025 as the population ages
- **Two candidate vaccines in development**
 - Phase I/II
- **Targets beta-amyloid**
 - Pivotal role in plaque formation

Nicotine addiction overview

Nicotine addiction

- **Nicotine conjugate vaccine (*NicVAX*)**
- **Over 1 billion smokers worldwide**
 - over 5 million tobacco-related deaths each year
- **Aid to smoking cessation and long-term abstinence**
- **Produces antibodies that bind to nicotine in the bloodstream**
 - prevents nicotine crossing the blood-brain barrier
- **Two Phase III studies ongoing**

GSK therapeutic vaccines: conclusions

- **ASCI represent a novel class of compounds based on tumour antigens**
 - Novel mechanism of action, tumour-specific, patient-selective
- **Proof of concept for activity demonstrated in double-blind, randomised, placebo-controlled Phase II in NSCLC**
- **Second proof of concept obtained independently in a Phase II in metastatic melanoma**
- **Data suggest investigational MAGE-A3 ASCI is well tolerated**
- **Potential biomarkers to select the patients who will benefit from the ASCI treatment have been identified in melanoma and in NSCLC**
- **Pivotal Phase III trials ongoing in NSCLC and melanoma, including biomarker validation**
- **Recent licensing agreements in Alzheimer's disease and nicotine addiction**



GlaxoSmithKline