



# NICE Guidelines and Access to Clinical Trials

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# What are NICE Guidelines?

- + The National Institute for Health and Care Excellence (NICE) provides national guidance and advice to improve health and social care
- + NICE Guidance applies to NHS England
  - + Scotland has an independent Scottish Medicines Agency
  - + Wales Assembly Government accepts NICE Guidance

# Different Types of NICE Guidance

- + NICE Technology Appraisal Guidance
  - + Recommendations on the use of new and existing medicines and treatments within the NHS
- + These can be:
  - + Medicines
  - + Medical Devices
  - + Diagnostic techniques
  - + Surgical procedures
  - + Health promotion activities

# Different Types of NICE Guidance

- + Clinical Guidelines
  - + Care for people with specific conditions
  - + Prevention, Diagnosis, Treatment, Longer term management
- + Public Health Guidelines
  - + Interventions to prevent disease and improve health
- + Social Care Guidelines
- + Medicines Practice Guidelines
- + Safe Staffing Guidelines
- + NICE Interventional Procedure Guidance

# Different Types of NICE Guidance

- + **Clinical Guidelines**

- + **Melanoma assessment and management guidelines**

- + **29 July 2015**

- + **Single Technology Appraisals**

- + **Melanoma drug treatments**

# NICE Melanoma Assessment and Management Guidelines, July 2015

- + British Association of Dermatology
  - + Revised Guidelines for the Management of Cutaneous Melanoma 2010
  - + Predate new systemic therapies
- + No pre-existing NICE Melanoma Management Guidelines
  - + Aim to reduce variation in practice and improve survival
  - + Intended for healthcare professionals & patients
  - + Not mandatory, but are used to develop national Quality Standards, which offer guidance for commissioning of services

# NICE Melanoma Assessment and Management Guidelines, July 2015

- + Addresses areas where there is uncertainty or variation in practice
  - + Assessing and staging melanoma, including use of SLNB
  - + Treating stages 0-4 melanoma
  - + Treating in-transit melanoma metastases
  - + Follow-up after treatment for melanoma
- + Advice on managing Vitamin D levels and drug therapy for intercurrent conditions in people diagnosed with melanoma

# NICE Melanoma Guidelines: Practice Change – Vitamin D

- + Measure vitamin D levels at diagnosis in all people with melanoma
- + Give people with suboptimal vitamin D levels supplementation

# NICE Melanoma Guidelines: Practice Change - SLNB

- + **Consider** sentinel lymph node biopsy (SLNB) as a staging procedure in people with stage IB – IIC melanoma with a Breslow thickness of >1mm
- + **Consider** completion lymphadenectomy for people whose sentinel lymph node biopsy shows micro-metastases

# NICE Melanoma Guidelines: Practice Change – surveillance scanning

- + **Consider** surveillance imaging as part of follow-up for people who have had stage IIC melanoma with SLNB or stage III melanoma and who become eligible for systemic therapy as a result of early detection of metastatic disease:
  - + **imaging 6 monthly for 3 years**

# NICE Melanoma Guidelines: Practice change – gene mutation testing

- + If targeted systemic therapy is an option, **offer** genetic testing
- + NICE Guidelines did not evaluate new immunotherapy and targeted therapies, as they are subject to NICE Technology Appraisals

# NICE Melanoma Guidelines: Practice Change – inclusion of ECT

- + Consider the following options as non-surgical treatment for in-transit metastases
  - + Systemic therapy
  - + Isolated limb infusion
  - + Isolated limb perfusion
  - + Radiotherapy
  - + Electrochemotherapy (ECT)
  - + CO<sub>2</sub> laser
  - + Imiquimod

# Quality Standards - What are They?

- + Quality Standards are generated following NICE Guidance
- + They set out the priority areas for quality improvement in health and social care
- + Quality Standards are not mandatory, but they can be used to plan and deliver services to provide the best possible care
- + Each standard provides
  - + A set of statements to help improve quality
  - + 3 dimensions of quality: safety, patient experience and clinical effectiveness
  - + Information on how to measure progress

# Management Guidelines for Non-cutaneous Melanoma

- + NICE Melanoma Guidelines covered cutaneous melanoma only
- + Uveal Melanoma National Guidelines, January 2015
  - + Supported by Melanoma Focus
  - + <http://melanomafocus.com/wp-content/uploads/2015/01/Uveal-Melanoma-National-Guidelines-Full-v5.3.pdf>
  - + Endorsed by NICE
- + Mucosal Melanoma Guidelines in Development
  - + Supported by Melanoma Focus

# Different Types of NICE Guidance

- + Clinical Guidelines
  - + Melanoma assessment and management guidelines
  - + 29 July 2015
- + **Single Technology Appraisals**
  - + Melanoma drug treatments

# NICE Technology Appraisals

- + Single Technology Appraisal (STA)
  - + Usually new pharmaceutical products or new indications of existing licensed products
  - + Aim to produce guidance soon after the technology is introduced in the UK
- + Multiple Technology Appraisal (MTA)
  - + Assesses several drugs or treatments used for 1 condition
- + Fast Track Appraisal (FTA) – new since 1 April 2017
  - + For technologies that offer exceptional value for money
  - + NHS England/commissioners will provide funding within 30 days of guidance publication (compared with standard 90 days)

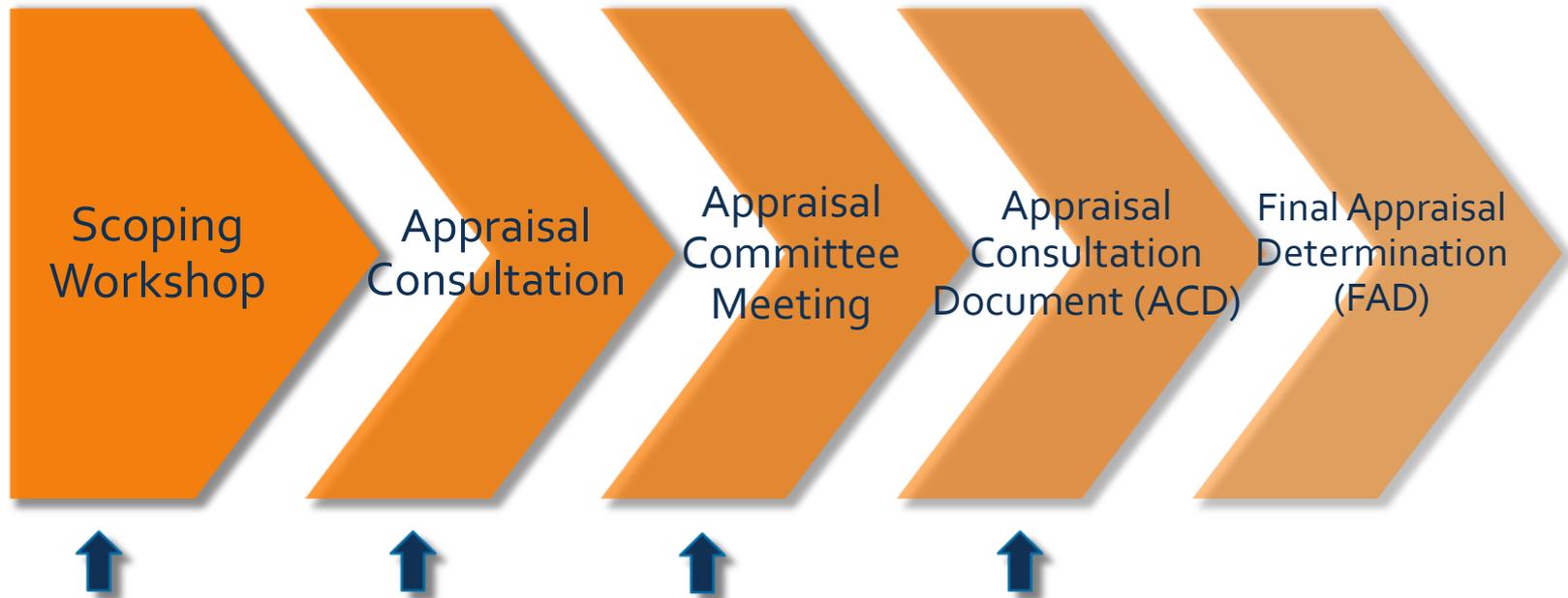
# NICE Technology Appraisals

- + Recommendations are based on:
  - + Clinical Evidence
    - + How well the medicine works
  - + Economic Evidence
    - + How well the medicine works in relation to how much it costs the NHS
    - + Does it represent value for money?

# NICE Technology Appraisal Process

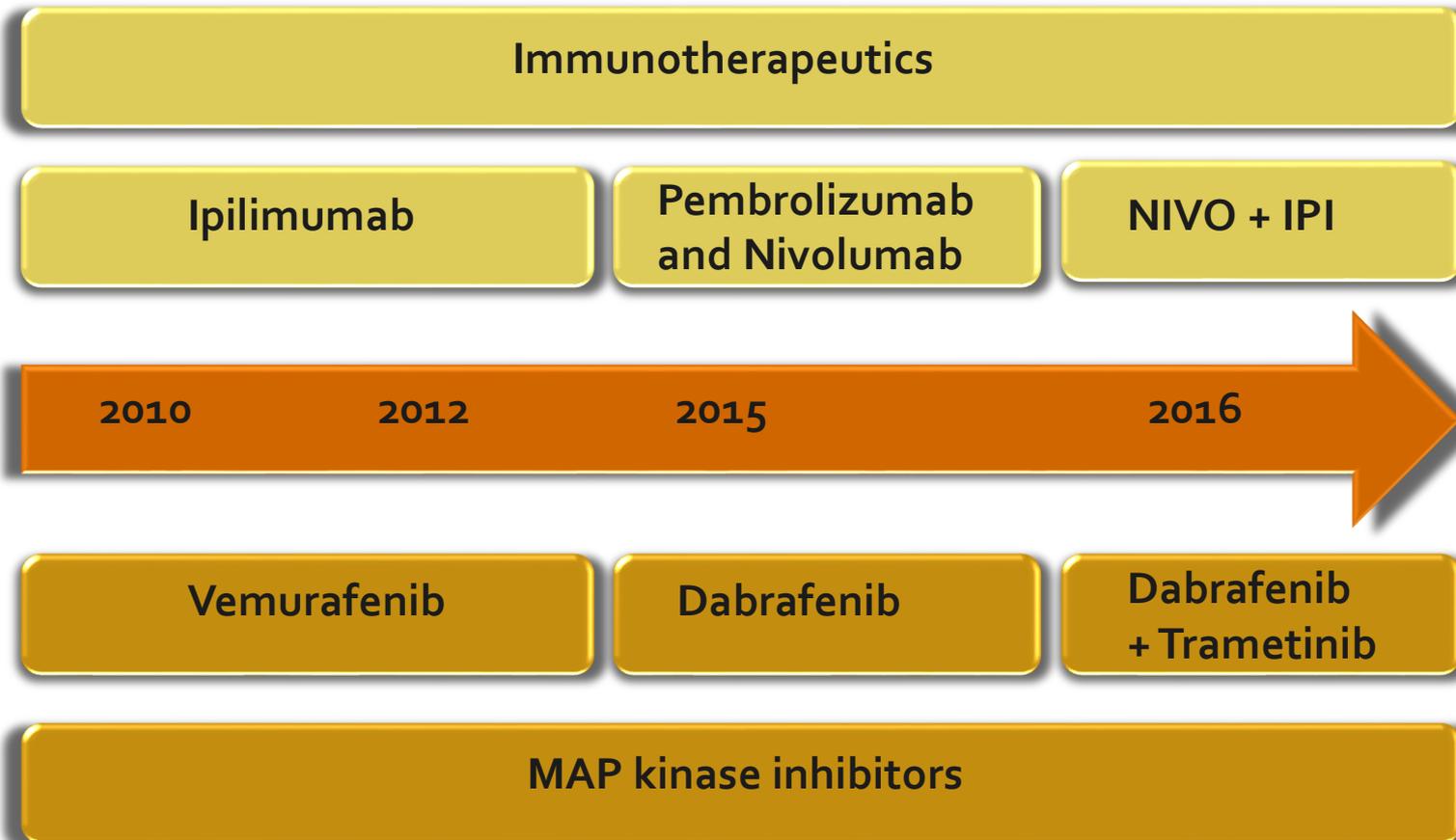


# NICE Technology Appraisal Process



Patient representatives, Clinical Experts, Manufacturer, Evidence Review Group (ERG)

# New Drug Treatments for Advanced Melanoma



# Translating NICE Guidance into Clinical Practice

- + NICE approvals are based on the Manufacturer Licensed Indication ('Marketing Authorisation')
- + Commissioners are required to provide funding for a positive STA within 90 days of publication
- + Since December 2016, clinicians must apply to prescribe all new high cost drugs via the national BlueTeq on-line registration system which was previously confined to CDF-listed drugs
- + *Health Warning: BlueTeq criteria may well restrict patient access*
  - + *Melanoma Working Group established to negotiate access criteria with NHS England*

# Why Clinical Trials?

- + Clinical trials provide the evidence that justifies change in practice
- + A drug treatment found to be effective in clinical trials will be given a license for use
- + NICE will only review licensed drugs and the clinical trial evidence will inform NICE guidance
- + Clinical trials offer patients a route to early access of state-of-the-art treatments
- + Not everyone taking part in a clinical trial directly benefits from doing so, but everyone taking part in a clinical trial directly contributes to helping future patients

# Vemurafenib: the first effective treatment for BRAF mutant metastatic melanoma showed activity in the very first patients treated

## The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

AUGUST 26, 2010

VOL. 363 NO. 9

### Inhibition of Mutated, Activated BRAF in Metastatic Melan

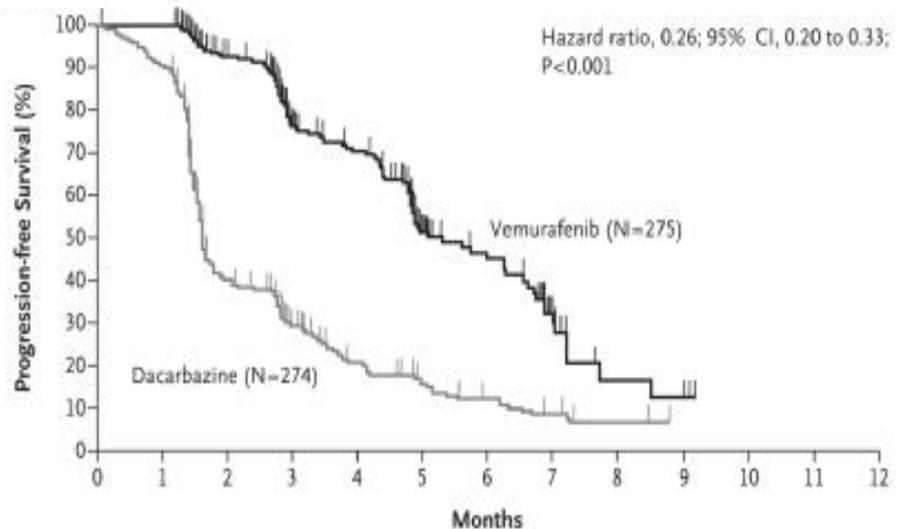
Keith T. Flaherty, M.D., Igor Puzanov, M.D., Kevin B. Kim, M.D., Antoni Ribas, M.D., Grant A. McArthur, M.B., B.S., Ph.D., Jeffrey A. Sosman, M.D., Peter J. O'Dwyer, M.D., Richard J. Lee, M.D., Joseph F. Grippo, Ph.D., Keith Nolop, M.D., and Paul B. Chapman, M.D.

#### ABSTRACT

Pre-treatment



At 15 weeks



Phase 1 trial

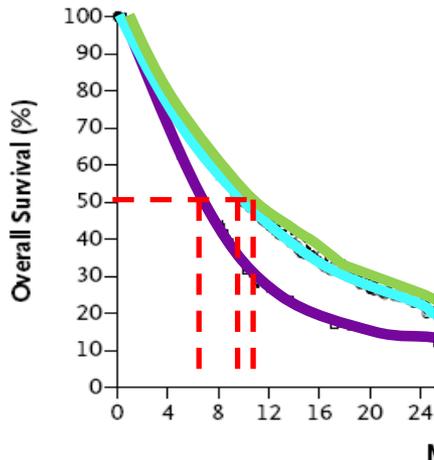


Phase 3 trial

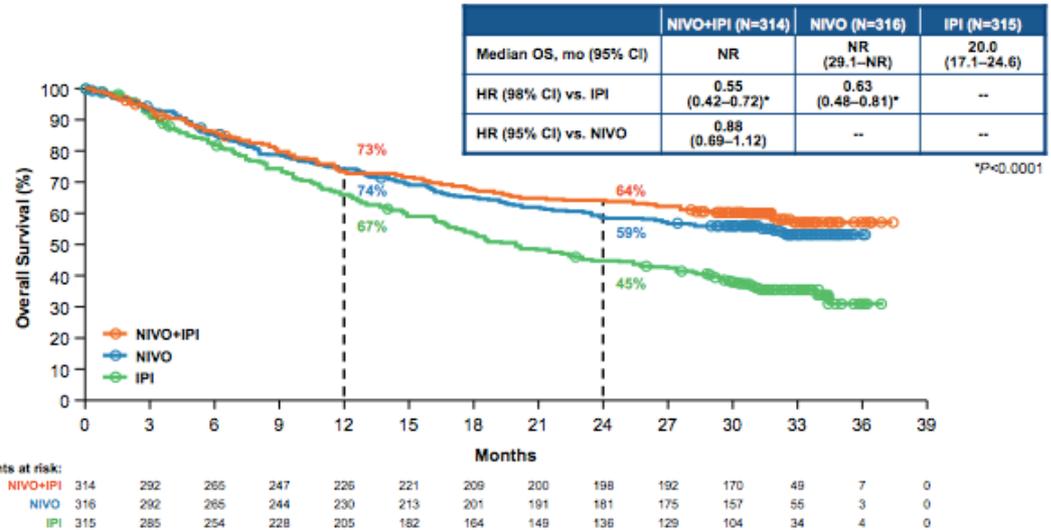
# Immune checkpoint inhibitors tested in clinical trials have improved survival of metastatic melanoma patients

— Ipi plus gp100    — Ipi    — gp100  
o o o Censored    x x x Censored    ■ ■ ■ Censored

Overall Survival



Overall Survival



# New Drug Treatments for Advanced Melanoma

## Immunotherapeutics

Ipilimumab

Pembrolizumab  
and Nivolumab

NIVO + IPI



Vemurafenib

Dabrafenib

Dabrafenib  
+ Trametinib

## MAP kinase inhibitors

# New Drug Treatments for Advanced Melanoma

## Immunotherapeutics

Ipilimumab

Pembrolizumab  
and Nivolumab

NIVO + IP

Life expectancy  
6-12 months

2012

2015

2016

Average  
Life expectancy  
3 years  
30% long term  
remissions

Vemurafenib

Dabrafenib

Dabrafe  
+ Trameti

## MAP kinase inhibitors

Year 2000:

for every **100** patients diagnosed with cancer in the UK, **4** entered a well-designed peer-reviewed clinical study

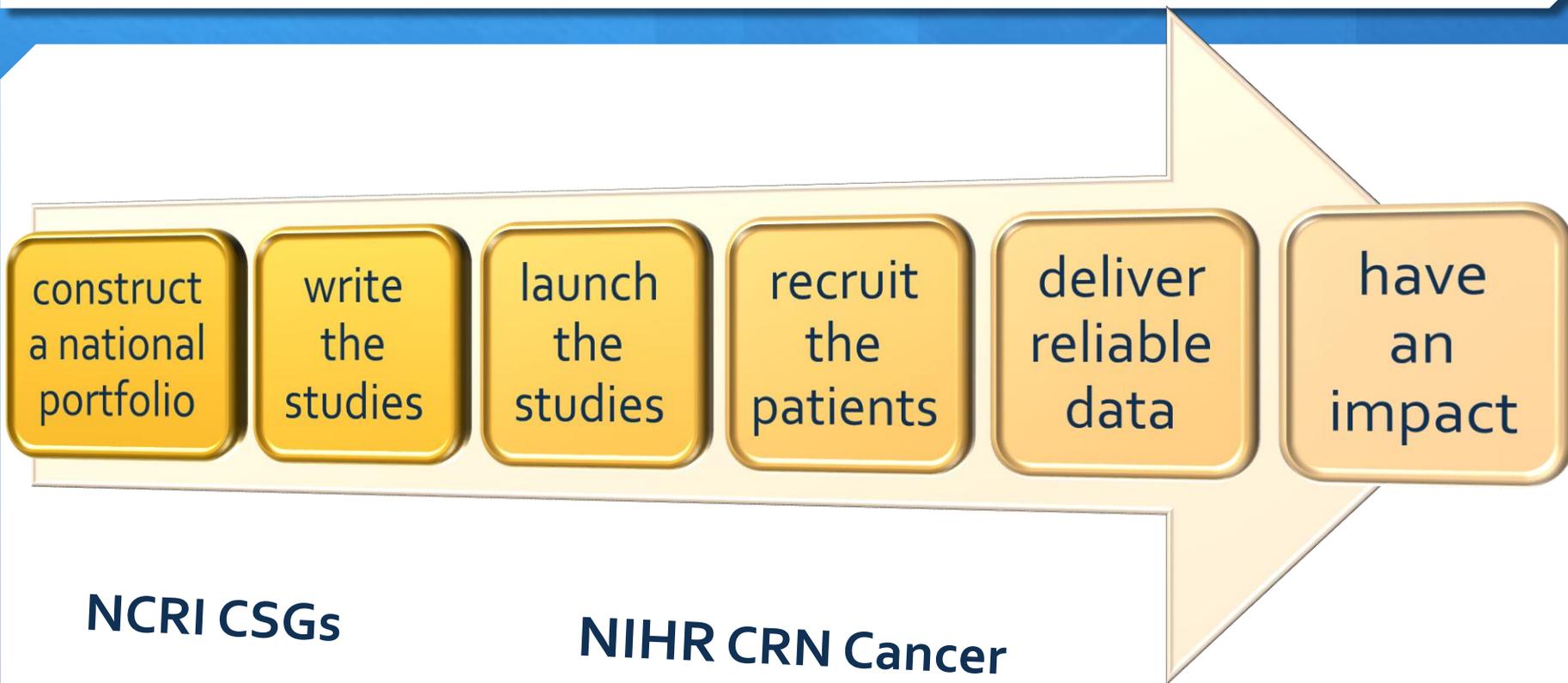


Year 2014:

for every **100** patients diagnosed with cancer in the UK, **20** entered a well-designed peer-reviewed clinical study



# National Infrastructure for Development and Delivery of Cancer Clinical Trials



# NCRI Skin Cancer Clinical Studies Group

## + Membership:

- + Oncologists
- + Dermatologists
- + Surgeon
- + Pathologist
- + Statistician
- + GP
- + Patient reps x 2

## Types of Trials:

- Commercial sponsored
- Non-commercial/academic/IIT
  
- Interventional
  - Drugs, radiotherapy, surgery
- Non-interventional
  
- Phase 1,2,3
  
- Screening
- Prevention
- Early Diagnosis
- Treatment

# How Can YOU Get Involved?

- + Access to clinical trials
  - + Clinical Trials Gateway
  - + <https://www.ukctg.nihr.ac.uk>

Try searching for a clinical trial You can search by condition or relevant keywords

melanoma

in

Cambridge, United Kingdom

Search

Can't find the trial you were looking for? [Sign up](#) to create a volunteer profile so that researchers can find you in the future

Your selection

Trial Status: Recruiting

From Me

50 Miles

Gender

Female (14)

Male (9)

Not Specified (73)

## Your search for **melanoma** in **Cambridge, United Kingdom** returned **93** trials

Sorted by Relevance

### **Melanoma** Image Analysis Algorithm (MIAA) Validation Study

Prospective, single-arm, cross-sectional, study to establish the effectiveness of MIAA to detect **melanoma** in pigmented lesions, compared to gold standard histological determination...

[Show More](#)

Recruiting

3 Locations

[See Trial Details](#)

**46.7**  
miles  
away

### MelmarT **Melanoma** Margins Trial Investigating 1cm v 2cm Wide Excision Margins for Primary Cutaneous **Melanoma**

**33.2**

# How Can YOU Get Involved?

- + Access to clinical trials
  - + Clinical Trials Gateway
    - + <https://www.ukctg.nihr.ac.uk>
  - + NCRI Portfolio Maps
    - + <https://csg.ncri.org.uk/homepage/portfolio-maps/>

# Skin Cancer

## Map A – Melanoma

↓ Click square below to reset map

	All melanomas	Cutaneous - BRAF mutant	Non - cutaneous		
	All	All	Mucosal ckit	Mucosal other	Uveal
1st line metastatic				PIANO Study	A Randomised th
	Pre/Op JX/594				
	The PERM Study BMS/936558				
					Melphalan/HDS
	NCRN545 MLN2480				
	Nivolumab 3 mg/kg in Combinati Keynote/ 252 (Pembro MK) Ti-061-101A				
		TRILOGY			
	CA209-915				
Adjuvant	The RTN2 Study ANZMTG 01.0				
Non-interv..	CR UK Stratifie				
	SC stem cells Serpina12 MISST OPAC				
	Malignant Melanoma-0456/0086				
	PASIP				
Surgery					
	Minitub (EORTC 1208) EAGLE FM				

Open Single CSG

Open Multi CSG

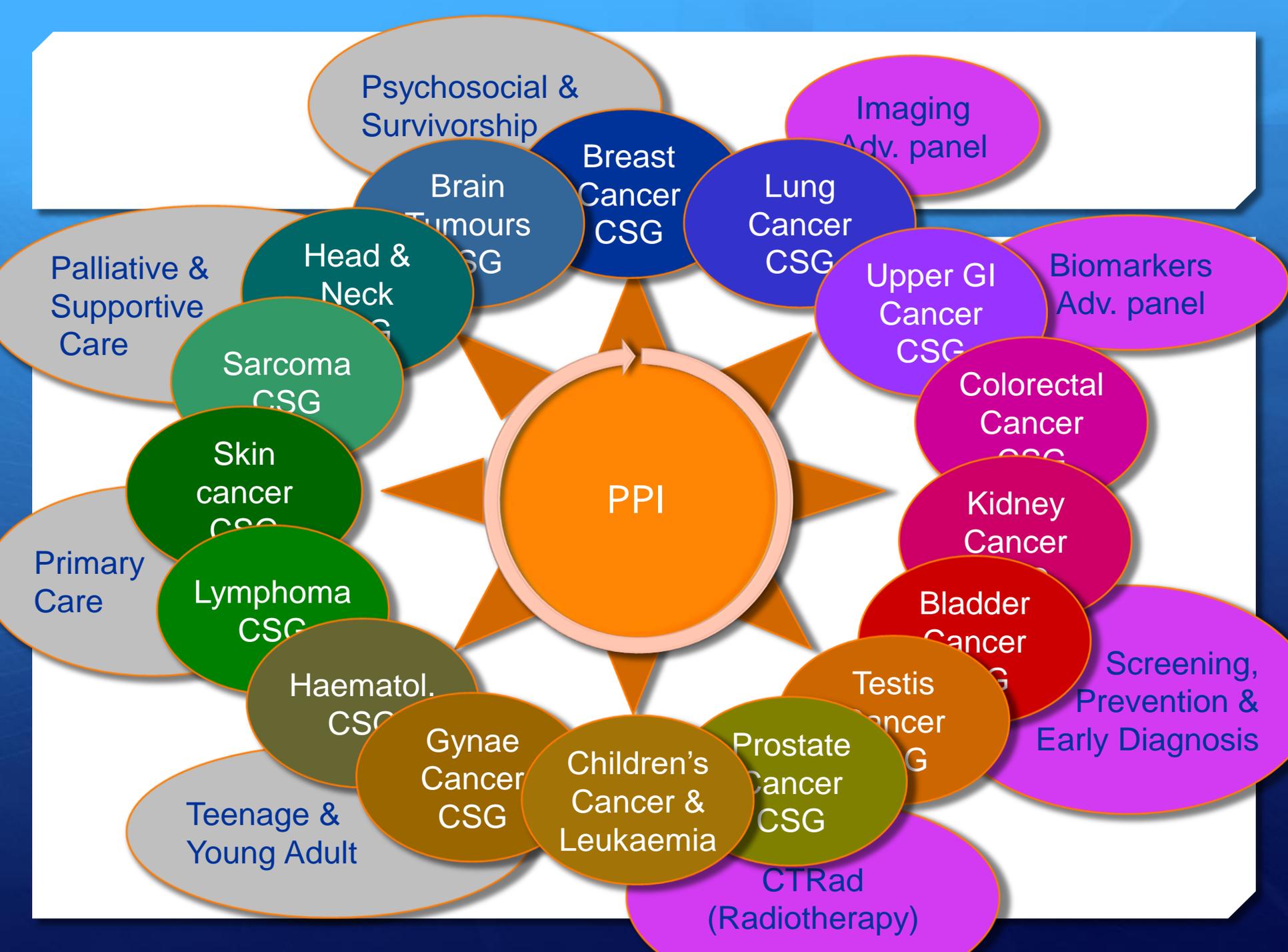
In Setup, Waiting NHS Permission Single CSG

In Setup, Waiting NHS Permission Multi CSG

In Setup, Waiting HRA Approval Single CSG

# How Can YOU Get Involved?

- + Access to clinical trials
  - + Clinical Trials Gateway
  - + <https://www.ukctg.nihr.ac.uk>
  - + NCRI Portfolio Maps
  - + <https://csg.ncri.org.uk/homepage/portfolio-maps/>
- + **Patient representatives needed**
  - + NCRI Clinical Studies Groups
  - + Local Research Networks



Psychosocial & Survivorship

Imaging Adv. panel

Breast Cancer CSG

Lung Cancer CSG

Brain Tumours CSG

Upper GI Cancer CSG

Biomarkers Adv. panel

Head & Neck CSG

Sarcoma CSG

Colorectal Cancer CSG

Palliative & Supportive Care

Skin cancer CSG

Kidney Cancer

Primary Care

Lymphoma CSG

Bladder Cancer

Haematol. CSG

Testis Cancer

Teenage & Young Adult

Gynae Cancer CSG

Children's Cancer & Leukaemia

Prostate Cancer CSG

Screening, Prevention & Early Diagnosis

CTRad (Radiotherapy)

PPI

**THANK YOU  
VERY MUCH!**



**YOU** *Make*  
*a Difference*