

Supplementary tables: the precision medicine approach to cancer therapy, part 1 — solid tumours

Table 1: Biomarkers important in breast cancer, the precision medicine (PM) agents used in this disease, and the companion diagnostic (CDx) tests used to select patients most likely to respond

Biomarkers	Agents used	Examples of companion diagnostic tests	Use of test results
ER	Anastrozole (Arimidex)	Immunohistochemistry ^{NHS} (IHC)	IHC is assessed as intensity (1–3) and proportion of cells stained (0–5) to provide a score of 0–8 (known as the Allred score)
	Exemestane (Aromasin)		
	Everolimus (Afinitor)	EndoPredict gene expression profiling assay (Myriad Genetics) ^{nNHS}	Identifies ER+ve tumours. Not cost effective for NHS
	Letrozole (Femara)		
	Fulvestrant (Faslodex)	Oncotype DX (Genomic Health Inc) ^{NHS}	Assesses whether a patient is likely to benefit from chemotherapy ⁶⁶
	Tamoxifen (Nolvadex)		
	Palbociclib (Ibrance)		
	Ribociclib (Kisqali)		
	Raloxifene Hydrochloride** (Evista)		
Toremifene* (Fareston)			
PgR	Everolimus (Afinitor)	EndoPredict Gene Expression Profiling Assay (Myriad Genetics) ^{nNHS}	Identifies PgR+ve tumours. Not considered to be cost effective for NHS
	Toremifene* (Fareston)	Oncotype DX (Genomic Health Inc) ^{nNHS}	Assesses whether a patient is likely to benefit from chemotherapy ⁶⁶ . Not considered to be cost effective for NHS

HER2/neu	Lapatinib*** (Tyverb)	Immunohistochemistry ^{NHS}	Score of 3+ defined as positive, 2+ equivocal
		HER2 IQFISH PharmDX assay ^{NHS} (Dako Omnis)	Used for direct confirmation of HER2 status, for example to check for amplification of HER2+ antigen in breast tumour cells after an equivocal HER2 IHC result of 2+
	Trastuzumab (Herceptin) Trastuzumab Emtansine (Kadcyla) Pertuzumab (Perjeta)	HercepTest (Dako PharmDx) — a semiquantitative IHC assay ^{NHS}	Used to select patients for treatment with trastuzumab and pertuzumab
Mutated <i>BRCA1</i> and <i>BRCA2</i>	Olaparib* (Lynparza)	BRCA Analysis CDx (Myriad Genetics Inc) ^{NHS} 68,69	Identifies ovarian cancer patients carrying germline <i>BRCA</i> mutations who may benefit from treatment with olaparib or talazoparib ⁷⁰
	Talazoparib** (BMN-673)		
CDK4 and CDK6	Abemaciclib (Verzenio) Palbociclib (Ibrance) Ribociclib (Kisqali)	None	-
PIK3CA	Alpelisib** (Piqray)	Qiagen's Therascreen PIK3CA RGQ PCR Kit	Used to detect mutations in PIK3CA found in breast cancer patients

* agents that are likely to be approved by National Institute for Health and Care Excellence (NICE) in the near future, but may not necessarily be used in the NHS^{40,71}

** agents that are unlicensed in the UK at the time of writing

*** agents that have been removed from NICE guidance or rejected by NICE

^{NHS} companion diagnostic tests which are used in the NHS based on cost/benefit ratio^{72,73}

^{nNHS} companion diagnostic tests which are not used in the NHS based on cost/benefit ratio^{72,73}

Table 2: Biomarkers important in lung cancer, the precision medicine (PM) agents used in this disease, and the companion diagnostic (CDx) tests used to select patients most likely to respond

Biomarkers	Agents used	Examples of companion diagnostic tests	Use of test results
Epidermal growth factor receptor tyrosine kinase (EGFR-TK) EGFR1/Human epidermal growth factor receptor 1 (HER1)	Gefitinib (Iressa) [‡]	The Cobas EGFR Mutation Test v2 ^{NHS} (Roche Molecular Systems, Inc) [‡]	Used to select patients with non-small cell lung cancer (NSCLC) who may benefit from gefitinib and erlotinib
	Erlotinib (Tarceva) [‡]		
EGFR/Erb-B family	Necitumumab ^{***} (Portrazza)	Thermo Fisher OncomineDx Target Test ^{NHS} (Thermo Fisher Scientific)	OncomineDx Target is a 23-gene test used to identify the best responders to agents working through the genes identified (i.e. EGFR, <i>BRAF</i> , <i>ALK</i> , <i>ROS-1</i> , <i>KRAS</i> and <i>NRAS</i>). It can also be used to monitor the presence or absence of variants in other genes ⁹¹⁻⁹³
EGFR (sensitivity toward T790M mutation) and with Exon 19 deletions or Exon 21 L858R mutations	Afatinib (Giotrif) [§]	EGFR Pharm Dx test (Dako Inc) ^{NHS} and the Therascreen EGFR RGQ PCR test (Qiagen) ^{NHS,94}	Both EGFR tests are used to guide the selection of patients who may benefit from treatment with afatinib
	Dacomitinib (Vizimpro)	Therascreen EGFR RGQ PCR Kit (Qiagen) ^{NHS,95}	This test detects exon deletions and insertions in the EGFR gene ⁹⁵
	Osimertinib (Tagrisso) ^Δ	The Cobas EGFR V2 test ^{NHS} (Roche Molecular Systems, Inc)	The V2 test is used to select NSCLC patients who may benefit from treatment with osimertinib
EGFR and HER2 (Exon 20 insertion mutation in EGFR)	Poziotinib ^{**} (also known as NOV120101 or HM781-36B) ⁹⁶	Thermo Fisher OncomineDx Target Test ^{NHS} (Thermo Fisher Scientific)	OncomineDx Target is a 23-gene test used to identify best responders to agents working through the genes identified (i.e. EGFR, <i>BRAF</i> , <i>ALK</i> , <i>ROS-1</i> , <i>KRAS</i> and <i>NRAS</i>). It can also be used to monitor the presence or absence of variants of other genes ⁹¹⁻⁹³
Anaplastic lymphoma kinase (<i>ALK</i>)	Ceritinib (Zykadia)	Ventana ALK (D5F3) Assay ^{NHS} (Novartis in collaboration with Roche)	Results from this test at the time of diagnosis can help determine whether patients may benefit from treatment with ceritinib and/or alectinib

	Alectinib (Alecensa)		
	Brigatinib (Alunbrig)	HTG EdgeSeq ALKPlus Assay EU ^{NHS} (HTG Molecular Diagnostics)	HTG EdgeSeq ALKPlus is an <i>in vitro</i> next-generation sequencing assay used to test for <i>ALK</i> status in NSCLC patients. It works in conjunction with the HTG EdgeSeq Analyser ⁹⁷
	Crizotinib (Xalkori)		
<i>ROS-1</i>	Crizotinib (Xalkori)	Thermo Fisher OncomineDx Target Test ^{NHS} (Thermo Fisher Scientific)	OncomineDx Target is a 23-gene test that can be used to identify potential best responders to crizotinib, and is also used to monitor for the presence or absence of variants of other genes ⁹¹⁻⁹³
	Lorlatinib (PF-6463922)		
Vascular endothelial growth factor (VEGFR), platelet-derived growth factor (PDGFR) and fibroblast growth factor (FGFR)	Nintedanib (Vargatef)	NexCourse Complete/Solid Test ^{NHS} (Genoptix Inc)	This test is used only to detect the mutation and not for drug selection
	Ramucirumab*** (Cyramza)		
<i>BRAF</i> ^{V600E/K}	Dabrafenib*** (Tafinlar)	Thermo Fisher OncomineDx Target Test ^{NHS} (Thermo Fisher Scientific)	OncomineDx Target is a 23-gene test that can be used to identify best responders to the genes identified (i.e. EGFR, <i>BRAF</i> , <i>ALK</i> , <i>ROS-1</i> , <i>KRAS</i> and <i>NRAS</i>), and also to detect the presence or absence of variants of other genes ⁹¹⁻⁹³

MEK	Trametinib*** (Mekinist)		
PD-L1 ^Δ	Pembrolizumab (Keytruda)	PD-L1 IHC 22C3 PharmDxTest ^{NHS} (Agilent Technologies/Dako Inc)	Used in the selection of patients who may benefit from treatment with pembrolizumab
	Nivolumab (Opdivo)	PD-L1 IHC 28-8 PharmDxTest ^{NHS} (Agilent Technologies/Dako Inc)	Used in the selection of patients who may benefit from treatment with nivolumab
	Durvalumab (Imfinzi)	The Ventana PD-L1 (SP263) Assay ^{NHS} using the Ventana BenchMark Ultra Instrument (Ventana Medical Systems Inc)	Used to select patients who may benefit from treatment with durvalumab
	Atezolizumab (Tecentriq)	None	-
	Avelumab** (Bavencio)	None	-
	Trametinumab** (CP-675,206)	None	-
TMB (not currently used in practice)	Ipilimumab** (Yervoy)	FoundationOne CDx ^{NHS} (FoundationFocus Inc) ⁹⁸	The FoundationOne CDx profiles 324 genes as well as microsatellite instability and TMB, and is used to identify potential best responders to 15 FDA-approved treatments Although it is not yet an approved companion diagnostic assay for TMB, it is being used experimentally to inform the clinical management of patients with respect to this biomarker ^{87,99}

*agents that are likely to be approved by National Institute for Health and Care Excellence (NICE) in the near

future, but may not necessarily be used in the NHS^{40,71}

** agents that are unlicensed in the UK at the time of writing

*** agents that have been removed from NICE guidance or rejected by NICE

^{NHS} companion diagnostic tests which are used in the NHS based on cost/benefit ratio^{72,73}

^{nNHS} companion diagnostic tests which are not used in the NHS based on cost/benefit ratio^{72,73}

‡Both gefitinib and erlotinib are first-generation TKIs

‡The Idylla™ EGFR Mutation Assay is used only for research and not for diagnostic purposes

§Afatinib is considered a second-generation inhibitor

△Osimertinib is considered a third-generation inhibitor. The decision by NICE to disallow the use of osimertinib for end-of-life consideration in this cancer type is being appealed by AstraZeneca (100)

⌒The PD-L1 assays described in this section can be used with more than one type of PD-L1 inhibitor

Table 3: Biomarkers important in metastatic colorectal cancer (mCRC), the precision medicine (PM) agents used in this disease and the companion diagnostic (CDx) tests used to select patients most likely to respond

Biomarkers	Agents used	Examples of companion diagnostic tests	Use of test results
<i>NRAS/KRAS</i>	Panitumumab (Vectibix)	Idylla NRAS-BRAF Mutation Test ^{NHS} (Biocartis/Amgen) ¹¹⁶	Used to help identify mCRC patients eligible for treatment with panitumumab based on a lack of mutations
		Cobas KRAS Mutation Test ^{NHS} (Roche Molecular Systems Inc)	Used to help identify mCRC patients who may benefit from treatment with cetuximab or panitumumab based on a lack of mutations
		Therascreen KRAS RGQ PCR Test ^{NHS} (Qiagen Ltd)	

	Cetuximab (Erbix)	Idylla ctKRAS Mutation Test ^{nNHS} (Biocartis/Merck) ¹¹⁷	Detects 21 mutations in the <i>KRAS</i> gene. The first liquid biopsy test to improve the selection of patients who may benefit from anti-EGFR therapies such as cetuximab ¹¹⁷ . Not considered to be cost effective by the NHS
HER3	Panitumumab (Vectibix)	Idylla NRAS-BRAF Mutation Test ^{nNHS} (Biocartis/Amgen) ¹¹⁶	Used to help identify mCRC patients suitable for treatment with panitumumab. Not considered to be cost effective for the NHS
VEGF-A	Bevacizumab*** (Avastin)	None	-
VEGFR2	Ramucirumab* (Cyramza)	None	-
VEGFR2-TIE2	Regorafenib (Stivarga)	None	-
UGT1A1	Irinotecan (Campto)	UGT1A1 Molecular Assay ^{nNHS} (Pfizer)	The presence of the polymorph UGT1A1*28 is associated with poor metabolism of the irinotecan metabolite (SN-38), and the need for a lower starting dose (or avoidance of treatment) due to potentially severe hematological toxicity

PD-L1 (some of the PD-L1 tests described can be used in association with different PD-L1 inhibitors)	Pembrolizumab* (Keytruda)	See entry for pembrolizumab in Table 2	See entry for pembrolizumab in Table 2
	Nivolumab* (Opdivo)	See entry for nivolumab in Table 2	See entry for nivolumab in Table 2
	Ipilimumab* (Yervoy)	FoundationOne CDx ^{NHS} (FoundationFocus Inc) ⁹⁸	The FoundationOne CDx test profiles 324 genes and is used to help identify potential best responders to 15 FDA-approved treatments. Although it is not formally recognised as a companion diagnostic kit for MSI-H and dMMR, it can be used to inform the clinical management of patients with respect to these biomarkers ⁸⁷
	Atezolizumab** (Tecentriq)	None	-

* agents that are likely to be approved by National Institute for Health and Care Excellence (NICE) in the near future, but may not necessarily be used in the NHS^{40,71}

** agents that are unlicensed in the UK at the time of writing

*** agents that have been removed from NICE guidance or rejected by NICE

^{NHS} companion diagnostic tests which are used in the NHS based on cost/benefit ratio^{72,73}

^{nNHS} companion diagnostic tests which are not used in the NHS based on cost/benefit ratio^{72,73}

Table 4: Biomarkers important in metastatic melanoma, the precision medicine (PM) agents used in this disease and the companion diagnostic (CDx) tests used to select patients most likely to respond

Biomarkers	Agents used	Examples of companion diagnostic tests	Use of test results
<i>BRAF</i> ^{V600}	Vemurafenib (Zelboraf)	Cobas 4800 <i>BRAF</i> V600 Mutation Test ^{NHS} (Roche Molecular Systems, Inc)	Indicates the presence of the <i>BRAF</i> ^{V600} mutation identifying patients suitable for treatment with vemurafenib
		Thermo Fisher Oncomine Dx Target Test ^{nNHS} (Thermo Fisher Scientific)	Identifies those patients who might best respond to <i>BRAF</i> inhibitors based on the profiling of 23 genes including <i>EGFR</i> , <i>BRAF</i> , <i>ALK</i> , <i>ROS-1</i> , <i>KRAS</i> and <i>NRAS</i> (91-93). Not considered to be cost-effective for the NHS
		Idylla <i>BRAF</i> Mutation Test ^{nNHS} (Biocartis, Inc)	Detects V600E/E2/D and V600K/R/M mutations in codon 600 of the <i>BRAF</i> gene, and is used to help identify patients who may benefit from <i>BRAF</i> inhibitors ¹²⁷ . Not considered to be cost effective for the NHS
<i>BRAF</i> ^{V600E/K}	Dabrafenib (Tafinlar)	THxID- <i>BRAF</i> CDx Test ^{#,NHS} (BioMérieux Inc)	Indicates the presence of V600E and V600K mutations in patients with unresectable or metastatic melanoma to select those who may benefit from treatment with dabrafenib and trametinib (or cobimetinib)
<i>MEK</i>	Trametinib (Mekinist) Cobimetinib*** (Cotellic)		
PD-L1	Pembrolizumab (Keytruda)	See entry for pembrolizumab in Table 2.	See entry for pembrolizumab in Table 2
	Nivolumab (Opdivo)	See entry for nivolumab in Table 2.	See entry for nivolumab in Table 2

CTLA-4	Ipilimumab (Yervoy)	None	-
--------	---------------------	------	---

*** agents that have been removed from National Institute for Health and Care Excellence (NICE) guidance or rejected by NICE

^{NHS} companion diagnostic tests which are used in the NHS based on cost/benefit ratio^{72,73}

^{nNHS} companion diagnostic tests which are not used in the NHS based on cost/benefit ratio^{72,73}

#In 2013 the FDA approved the use of dabrafenib and trametinib in combination alongside the THxID BRAF test from BioMérieux. It is the second companion diagnostic approved by the FDA for *BRAF* mutation detection following approval of Roche's Cobas 4800 BRAF V600 Mutation Test in 2011

Table 5: Biomarkers important in ovarian cancer, the precision medicine (PM) agents used in this disease and the companion diagnostic (CDx) tests used to select patients most likely to respond

Biomarkers	Agents used	Examples of companion diagnostic tests	Use of test results
Mutated <i>BRCA1</i> and <i>BRCA2</i>	Niraparib (Zejula)	BRACAnalysis CDx ^{NHS} (Myriad Genetics Inc)	Identifies ovarian cancer patients carrying germline <i>BRCA</i> mutations who should respond to niraparib
	Olaparib (Lynparza)	BRCA Analysis CDx (Myriad Genetics Inc) ^{NHS,68,69}	Identifies ovarian cancer patients carrying germline <i>BRCA</i> mutations who may benefit from treatment with olaparib ⁷⁰
	Rucaparib (Rubraca)	FoundationFocus CDxBRAC ^{NHS} (Foundation Medicine Inc)	Identifies advanced ovarian cancer patients with mutations in their <i>BRCA1</i> and <i>BRCA2</i> genes who are likely to benefit from treatment with rucaparib
VEGFR1 and VEGFR2	Bevacizumab (Avastin)	None	-
CA125 and CA125 II	None	Test kits, based on ELISA, are under development in collaboration between Morphotek Inc and Fujirebio Diagnostics	CA125 and CA125 II are diagnostic biomarkers for ovarian cancer

^{NHS} companion diagnostic tests which are used in the NHS based on cost/benefit ratio^{72,73}

Table 6: Biomarkers important in prostate cancer, the precision medicine (PM) agents used in this disease and the companion diagnostic (CDx) tests used to select patients most likely to respond

Biomarkers	Agents used	Examples of companion diagnostic tests	Use of test results
AR (Androgen Receptor)	Apalutamide* (Erleada)	Numerous commercial test kits available.	There is currently no screening program for prostate cancer in the UK, as benefits have not been proven to outweigh the risks ¹⁴⁷
	Abiraterone (Zytiga)	-	N/A
	Enzalutamide (Xtandi)	-	N/A
	Darolutamide** (Nubeqa)	-	N/A
Mutated <i>BRCA1</i> and <i>BRCA2</i>	Olaparib** (Lynparza)	See Table 5 for examples of companion diagnostic tests available for <i>BRCA1</i> and <i>BRCA2</i>	BRCA1/2 analysis has been used experimentally to identify prostate cancer patients who are likely to respond to PARP inhibitors such as olaparib

* agents that are likely to be approved by National Institute for Health and Care Excellence (NICE) in the near future, but may not necessarily be used in the NHS^{40,71}

** agents that are unlicensed in the UK at the time of writing

Table 7: Biomarkers important in renal cancer, the precision medicine (PM) agents used in this disease and the companion diagnostic (CDx) tests used to select patients most likely to respond

Biomarkers	Agents used	Examples of companion diagnostic tests	Use of test results
VEGFR 1–3 and PDGFR α/β	Pazopanib (Votrient)	NexCourse ^{nNHS} Complete/Solid Genoptix-A (Novartis Inc)	Over-expression of VEGFR 1–3 is detected and allows the selection of patients for treatment with Pazopanib
	Sunitinib (Sutent)	LC-MS/MS ^{NHS}	Within the NHS, plasma levels of the active metabolite of Sunitinib (i.e. N-

			desmethylsunitin-ib) are measured to assess adherence and optimise treatment
	Lenvatinib (Lenvima)	None	-
	Tivozanib (Fotivda)	None	-
	Sorafenib (Nexavar)	None	-
	Everolimus (Afinitor)	None	-
	Temsirolimus (Torisel)	None	-
VEGFR 1-3	Axitinib (Inlyta)	None	-
	Cabozantinib (Cabometyx)	None	-
PD-L1	Pembrolizumab* (Keytruda)	See entry for pembrolizumab in Table 2	See entry for pembrolizumab in Table 2
	Nivolumab (Opdivo)	See entry for nivolumab in Table 2	See entry for nivolumab in Table 2
	Atezolizumab** (Tecentriq)	None	-

* agents that are likely to be approved by National Institute for Health and Care Excellence (NICE) in the near future, but may not necessarily be used in the NHS^{40,71}

** agents that are unlicensed in the UK at the time of writing

^{NHS} companion diagnostic tests which are used in the NHS based on cost/benefit ratio^{72,73}

^{nNHS} companion diagnostic tests which are not used in the NHS based on cost/benefit ratio^{72,73}

Table 8: Biomarkers important in hepatocellular carcinoma, the precision medicine (PM) agents used in this disease, and the companion diagnostic (CDx) tests used to select patients most likely to respond

Biomarkers	Agents used	Examples of companion diagnostic tests	Use of test results
VEGFR and PDGFR	Sorafenib (Nexavar)	Sorafenib by LC-MS/MS ^{NHS}	Measures the active metabolite of Sorafenib (Sorafenib N-oxide) in plasma to assess adherence, monitor toxicity and optimise treatment

	Lenvatinib (Lenvima)	None	-
	Regorafenib (Stivarga)	None	-
VEGFR	Cabozantinib (Cometriq)	None	-
	Vandetanib** (Caprelsa)	None	-
PD-L1	Nivolumab** (Opdivo)	See entry for nivolumab in Table 2	See entry for nivolumab in Table 2

** agents that are unlicensed in the UK at the time of writing

NHS companion diagnostic tests which are used in the NHS based on cost/benefit ratio^{72,73}

Table 9: Biomarkers used in medullary and papillary thyroid cancers, the precision medicine (PM) agents used in this disease, and the companion diagnostic (CDx) tests used to select patients most likely to respond

Biomarkers	Agents used	Examples of companion diagnostic tests	Use of test results
VEGFR and PDGFR	Sorafenib (Nexavar)	See entry for Sorafenib in Table 8	See entry for Sorafenib in Table 8
	Lenvatinib (Lenvima)	None	-
	Regorafenib** (Stivarga)	None	-
VEGFR	Cabozantinib (Cometriq)	None	-
	Vandetanib (Caprelsa)	None	-
<i>BRAF</i> ^{V600}	Dabrafenib** (Tafinlar) Trametinib** (Mekinist)	See entry for Dabrafenib and Trametinib in Table 4	See entry for Dabrafenib and Trametinib in Table 4

** agents that are unlicensed in the UK at the time of writing

Table 10: Biomarkers used in pancreatic neuroendocrine tumours (PNTs), the precision medicine (PM) agents used in this disease, and the companion diagnostic (CDx) tests used to select patients most likely to respond

Biomarkers	Agents used	Examples of companion diagnostic tests	Use of test results
VEGF	Everolimus (Afinitor)	Tandem mass spectrometric (LC-MS/MS) assay for measuring everolimus ^{NHS}	Due to a narrow therapeutic index, plasma concentrations of everolimus must be routinely monitored, usually on a pre-dose (trough) sample
VEGFR, VEGFR2 and PDGFR α/β	Sunitinib (Sutent)	See entry for Sunitinib in Table 7	See entry for Sunitinib in Table 7
	Vandetanib** (Caprelsa)	None	-
	Erlotinib** (Tarceva)	None	-
UGT1A1	Nano-Liposomal Irinotecan*** (Onivyde)	See entry for Irinotecan in Table 3	See entry for Irinotecan in Table 3
<i>BRCA1</i> and <i>BRCA2</i>	Olaparib* (Lynparza)	See Table 5 for examples of companion diagnostic tests available for <i>BRCA1</i> and <i>BRCA2</i>	See Table 5 for examples of companion diagnostic tests available for <i>BRCA1</i> and <i>BRCA2</i>

** agents that are unlicensed in the UK at the time of writing

*** agents that have been removed from National Institute for Health and Care Excellence (NICE) guidance or rejected by NICE

^{NHS} companion diagnostic tests which are used in the NHS based on cost/benefit ratio^{72,73}

Table 11: The main biomarker used in bladder cancer, the precision medicine (PM) agents used in this disease, and the companion diagnostic (CDx) tests used to select patients most likely to respond

Biomarkers	Agents used	Examples of companion diagnostic tests	Use of test results
PD-L1	Durvalumab** (Imfinzi)	See entry for Durvalumab in Table 2	See entry for Durvalumab in Table 2
	Atezolizumab** (Tecentriq)	None	-

	Avelumab** (Bavencio)	None	-
FGFR	Erdafitinib** (Balversa)	Therascreen FGFR RGQ RT-PCR Kit ^{nNHS} (Qiagen)	This testing kit is used to identify patients who may benefit from erdafitinib

** agents that are unlicensed in the UK at the time of writing

^{nNHS} companion diagnostic tests which are not used in the NHS based on cost/benefit ratio^{72,73}

Table 12: The main biomarker relevant to basal cell carcinoma, and the small molecule inhibitors associated with it

Biomarker	Agents used	Examples of companion diagnostic tests	Use of test results
Hedgehog signaling pathway	Vismodegib (Erivedge)	None	-
	Sonidegib** (Odomzo)	None	-

** agents that are unlicensed in the UK at the time of writing

Table 13: The main biomarkers relevant to gastrointestinal stromal tumours, the precision medicine (PM) agents used in this disease, and the companion diagnostic (CDx) tests used to select patients most likely to respond

Biomarkers	Agents used	Examples of companion diagnostic tests	Use of test results
C-Kit (also known as CD117) or DOG1	Imatinib (Glivec)	None	-
	Sunitinib (Sutent)	See entry for Sunitinib in Table 7	See entry for Sunitinib in Table 7
	Regorafenib (Stivarga)	None	-
PDGFRA	Sunitinib (Sutent)	See entry for Sunitinib in Table 7	See entry for Sunitinib in Table 7
	Regorafenib (Stivarga)	None	-

Table references

- ⁴⁰Jamieson AM, Yu S, Annicelli CH & Medzhitov R. Influenza virus-induced glucocorticoids compromise innate host defense against a secondary bacterial infection. *Cell Host Microbe* 2010;7(2):103–114. doi: 10.1016/j.chom.2010.01.010
- ⁶⁶GenomeWeb. UK's NHS adopts NICE advice to provide oncotype DX for intermediate risk breast cancer patients. New York: GenomeWeb. 2015. Available at: https://www.genomeweb.com/cancer/uks-nhs-adopts-nice-advice-provide-oncotype-dx-intermediate-risk-breast-cancer-patients?utm_source=TrendMD&utm_medium=TrendMD&utm_campaign=0 (accessed September 2019)
- ⁶⁸GenomeWeb. Myriad genetics submits supplementary PMA for BRACAnalysis CDx. New York: GenomeWeb. 2018. Available at: https://www.genomeweb.com/molecular-diagnostics/myriad-genetics-submits-supplementary-pma-bracanalysis-cdx?utm_source=Sailthru&utm_medium=email&utm_campaign=GWDN Mon AM 2018-06-18&utm_term=GW (accessed September 2019)
- ⁶⁹GenomeWeb. FDA accepts myriad BRACAnalysis CDx supplementary PMA for lynparza in breast cancer indication. New York: GenomeWeb. 2017. Available at: https://www.genomeweb.com/regulatory-news/fda-accepts-myriad-bracanalysis-cdx-supplementary-pma-lynparza-breast-cancer?utm_source=Sailthru&utm_medium=email&utm_campaign=GWDN Wed AM 2017-10-18&utm_term=GW Daily News Bulletin (accessed September 2019)
- ⁷⁴National Institute for Health and Care Excellence. Guidance and advice list. 2017. Available at: <https://www.nice.org.uk/guidance/published?type=ta>
- ⁷²Viapath. Test index. Online: Viapath. 2014. Available at: <http://www.viapath.co.uk/tests-index> (accessed September 2019)
- ⁷³Viapath. New tests. Online: Viapath. 2013. Available at: <http://www.viapath.co.uk/new-tests> (accessed September 2019)
- ⁸⁷Ray T. BMS immunotherapy combo study backs FoundationOne CDx tumor mutational burden indication. New York: GenomeWeb. 2018. Available at: https://www.genomeweb.com/molecular-diagnostics/bms-immunotherapy-combo-study-backs-foundationone-cdx-tumor-mutational-burden?utm_source=Sailthru&utm_medium=email&utm_campaign=GWDN Fri AM 2018-02-09&utm_term=GW Daily News Bulletin (accessed September 2019)
- ⁹¹GenomeWeb. Cancer genetics gets NY state approval for Thermo Fisher lung cancer CDx. New York: GenomeWeb. 2017. Available at: https://www.genomeweb.com/molecular-diagnostics/cancer-genetics-gets-ny-state-approval-thermo-fisher-lung-cancer-cdx?utm_source=Sailthru&utm_medium=email&utm_campaign=GWDN Tues AM 2017-12-19&utm_term=GW Daily News Bulletin (accessed September 2019)
- ⁹²Ray T. After approval of next-gen sequencing CDx panel, Thermo Fisher seeks rapid expansion of indications. New York: GenomeWeb. 2017. Available at: <https://www.genomeweb.com/clinical-sequencing/after-approval-next-gen-sequencing-cdx-panel-thermo-fisher-seeks-rapid-expansion> (accessed September 2019)
- ⁹³GenomeWeb. Quest to offer Thermo Fisher's Oncomine Dx target test. New York: 360Dx. 2018. Available at: https://www.genomeweb.com/clinical-lab-management/quest-offer-thermo-fishers-oncomine-dx-target-test?utm_source=Sailthru&utm_medium=email&utm_campaign=GWDN Wed AM 2018-02-07&utm_term=GW Daily News Bulletin (accessed September 2019)
- ⁹⁴GenomeWeb. Qiagen gets FDA OK for Expanded use of EGFR CDx for lung cancer drug. New York: GenomeWeb. 2018. Available at: https://www.genomeweb.com/pcr/qiagen-gets-fda-ok-expanded-use-egfr-cdx-lung-cancer-drug?utm_source=Sailthru&utm_medium=email&utm_campaign=GWDN Fri AM 2018-01-19&utm_term=GW Daily News Bulletin (accessed September 2019)
- ⁹⁵GenomeWeb. FDA approves expanded use of Qiagen EGFR CDx in lung cancer. New York: GenomeWeb. 2018. Available at: <https://www.genomeweb.com/regulatory-news/fda-approves-expanded-use-qiagen-egfr>

cdx-lung-cancer?utm_source=Sailthru&utm_medium=email&utm_campaign=GWDN Fri AM 2018-09-28&utm_term=GW Daily News Bulletin - .W69SiC3GxTZ (accessed September 2019)

⁹⁶GenomeWeb. Thermo Fisher inks new pharma partnerships to expand CDx use of Oncomine NGS test. Online: GenomeWeb. 2018. Available at: https://www.genomeweb.com/molecular-diagnostics/thermo-fisher-inks-new-pharma-partnerships-expand-cdx-use-oncomine-ngs-test?utm_source=Sailthru&utm_medium=email&utm_campaign=GW MDx Thurs 2018-05-03&utm_term=Molecular Diagnostics Bulletin (accessed September 2019)

⁹⁷HTG EdgeSeq ALKPlus assay EU for ALK status testing in non-small-cell lung cancer. Medtech innovation briefing [MIB128] (2017).

⁹⁸Foundation Medicine I, inventor; FoundationOne, assignee. FoundationOne CDx™- Technical information. USA2017 30 November 2017.

⁹⁹Ashford M. With promising data in early-stage NSCLC, PGDx continues TMB test kit development. Online: GenomeWeb. 2018. Available at: https://www.genomeweb.com/cancer/promising-data-early-stage-nsclc-pgdx-continues-tmb-test-kit-development?utm_source=Sailthru&utm_medium=email&utm_campaign=GWDN Mon PM 2018-04-30&utm_term=GW Daily News Bulletin (accessed September 2019)

¹¹⁶Biocartis, Amgen sign CDx development deal for Idylla RAS biomarker tests. New York: GenomeWeb. 2017. Available at: https://www.genomeweb.com/business-news/biocartis-amgen-sign-cdx-development-deal-idylla-ras-biomarker-tests?utm_source=Sailthru&utm_medium=email&utm_campaign=GWDN Mon AM 2017-12-04&utm_term=GW Daily News Bulletin (accessed September 2019)

¹¹⁷Biocartis gets CE marking for two colorectal cancer liquid biopsy tests. New York: GenomeWeb. 2017. Available at: https://www.genomeweb.com/pcr/biocartis-gets-ce-marking-two-colorectal-cancer-liquid-biopsy-tests?utm_source=Sailthru&utm_medium=email&utm_campaign=GW Cancer Mon 2017-11-27&utm_term=Cancer Bulletin (accessed September 2019)

¹²⁷Inc B. Technical sheet Idylla™ BRAF Mutation Test. In: Inc B, editor. Online. 1 ed. Online: Biocartis Inc; 2016. 1–3.