Supplementary Material

Influence of gut microbiota in anticancer therapies (including in breast cancer).

Chemotherapy	Anthracyclines				
	Doxorubicin	Pharmacokinetics	*Raoultellaplanticola*	*R. planticola*: doxorubicin deglycosylation into 7-deoxydoxorubicinol 7-deoxydoxorubicinolone	68
			Escherichia coli BW25113 *Klebsiella pneumoniae*	Doxorubicin degradation dependent on molybdopterin-dependent enzymes	
		Toxic effects	*Raoultellaplanticola*	↓cardiotoxicity and other side-effects	
	Alkylating agents				
	Cyclophosphamide	Pharmacokinetics	*Enterococcus hirae* *Lactobacillus johnsonii* *Lactobacillus murinus*	↑ gut barrier permeability	64 69 70
				↑bacteria translocation to lymphoid organs	
				↑Th1 and Th17 cells	
				↑ level of IFN-γ and IL-17	
				↑ antitumour immunological response	
		Toxic effects	No studies available		
	Taxanes				
	Paclitaxel	Pharmacokinetics	No studies available*		
		Toxic effects	*Akkermansiamuciniphila*	↓ systemic inflammation and taxanes-induced neuropathic pain.	71
			Eubacterium siraeum *Lactobacillus intestinalis*	Inhibitors of pain phenotype	
	Docetaxel	Pharmacokinetics	No studies available*		
		Toxic effects	*Bifidobacterium breve* strain Yakult *Lactobacillus casei* strain Shirota Galactooligosaccharides	↓ severity: diarrhoea, lymphopenia and febrile neutropenia	64 72
	Deoxycytidine analogues				
	Gemcitabine	Pharmacokinetics	Gammaproteobacteria	↓efficacy gemcitabine → Inactive form (nucleoside analogue-catabolising enzymes)	64 73
		Toxic Effects	*Mycoplasma* spp.		
	Pyrimidine analogues				
	5-fluorouracil **Capecitabine**	Pharmacokinetics	*Mycoplasma hyorhinis*	↓cytostatic activity (FdUrd and F3(d)Thd) ↑ cytostatic activity (5′dFUrd)	64 76 77
		Toxic effects		↓toxicityafter FMT from healthy mice	
	Antimitotic agents				
	Eribulin	Pharmacokinetics	*Akkermansia* *Faecalibacterium*	Shift in abundance after 2 cycles	92
		Toxic effects			

Anti - HER 2	HER2 inhibitors					
	Trastuzumab	Pharmacokinetics	Clostridiales	↑efficacy (including ↑pCR)		80
			Lactococcus lactis *Lactobacillus paracasei*			
			Bacteroidales	↓efficacy		
		Toxic effects	No studies available*			
	Pertuzumab	Pharmacokinetics	No studies available*			
		Toxic effects		Rifaximin: ↓ PIGO		81
	Trastuzumab emtansine	Pharmacokinetics	No studies available*			
		Toxic effects	No studies available*			
	Neratinib	Pharmacokinetics	No studies available*			
		Toxic effects	No studies available*			
	Tucatinib	Pharmacokinetics	No studies available*			
		Toxic effects	No studies available*			
Hormonal therapy	Selective oestrogen modulators/degraders					
	Tamoxifen	Pharmacokinetics		↓ BC risk: Tamoxifen + Daidzein		83
				↓ BC risk: Tamoxifen + Genistein		
		Toxic effects	No studies available*			
	Raloxifen	Pharmacokinetics	No studies available*			
		Toxic effects	No studies available*			
	Fulvestrant	Pharmacokinetics	No studies available*			
		Toxic effects	No studies available*			
	Aromatase inhibitors					
	Letrozole	Pharmacokinetics		↓Bacteroidales ↑↓Firmicutes	↑increasedadiposity	82
		Toxic effects	No studies available*			
	Anastrozole	Pharmacokinetics	No studies available*			
		Toxic effects	No studies available*			
	Exemestane +/- everolimus (mTOR kinase inhibitor)	Pharmacokinetics	No studies available*			
		Toxic effects	No studies available*			
	GnRH agonists					
	Goserelin	Pharmacokinetics	No studies available*			
		Toxic effects	No studies available*			
	Leuprorelin	Pharmacokinetics	No studies available*			
		Toxic effects	No studies available*			
	Triptorelin	Pharmacokinetics	No studies available*			
		Toxic effects	No studies available*			
r dr	Cyclin inhibitors					

		Pharmacokinetics	No studies available*			
		Toxic effects	No studies available*			
	PARP inhibitors					
		Pharmacokinetics	No studies available*			
		Toxic effects	No studies available*			
Immunotherapy	Anti-PD-1					
	Nivolumab Pembrolizumab	Pharmacokinetics	↑*Bacteroidescaccae* ↑*Bifidobacteriumlongem* ↑*Collinsellaaerofaciens* ↑*Enterococcusfaecium* ↑*Faecalibacteriumprausnitzii* ↑*Lachnospiraceae* ↑*Veillonellaceae*	↑systemic and antitumour immunity		64 80 88 89 90 91
			↑*Ruminococcaceae*	↑efficacy with FMT from responders		
			↑Microbiota diversity			
		Toxic effects	No studies available*			
	Anti-PD-L1					
		Pharmacokinetics	*Akkermansiamuciniphila* *Bifidobacterium*	↑T cell response		80 89 90 91
		Toxic effects	No studies available*			
	Anti-CTLA-4					
	Ipilimumab	Pharmacokinetics	*Bacteroidescaccae* *Bacteroidesfragilis* *Bacteroidesthetaiotaomicron*	↑efficacy by Th1 immune response		64 80 85 86
		Toxic effects	*Bacteroidaceae* *Barnesiellaceae* *Rikenellaceae*	↓ levels of bacteria		64 85
				↓ polyamine transport		
				↓ vitamin B biosynthesis		
				↑risk of colitis		
Radiotherapy	Radiotherapy					
		Pharmacokinetics	*Rubrobacterradiotolerans*	D10 value	11,000 Gy	Radioresistant effect	98
			Deinococcusradiodurans R1		10,000 Gy		
			Rubrobacterxylanophilus		5,500 Gy		
			*Chroococcidiopsis*spp.		4,000 Gy		
			Hymenobacteractinosclerus		3,500 Gy		
			Kineococcusradiotolerans		2,000 Gy		
			Acinetobacter radioresistens		2,000 Gy		
			Kocuria rosea		2,000 Gy		
			Methylobacteriumradiotolerans		1,000 Gy		
		Toxic effects	*Bifidobacterium* spp. *Lactobacillus sakei* *Lactobacillus acidophilus* *Lactobacillus casei*	Radioprotective effect			97

			↓ Firmicutes ↑*Akkermansia* ↑*Bacteroides* ↑*Parabacteroides* ↑*Sutterella* ↑*Turicibacter* ↑genus RF32 order	Late radiation-tissue injury ↑IL-1β, IL-6 and TNF-α	101

BC (breast cancer); CTLA-4 (cytotoxic T-lymphocyte–associated antigen 4); D10 value (dose needed to eradicate 90% of irradiated population); F3(d)Thd (5-trifluorothymidine); FdUrd (5-fluoro-2'-deoxyuridine); 5-fluoro-5′-deoxyuridine (5′dFUrd); FMT (faecal microbiota transplant); GnRH (gonadotropin-releasing hormone); Gy (Gray); HER2 (human epidermal growth factor 2); IFN-γ (interferon-gamma); IL (interleukin); mTOR (mammalian target of rapamycin); PARP (poly-ADP ribose polymerase); pCR (pathological complete response); PD-L1 (programmed death-ligand 1); PIGO (pertuzumab-induced gastrointestinal toxicity); Th (T helper); TNF-α (tumour necrosis factor-alpha). Peach colour (chemotherapy agents); green colour (HER2 inhibitors); yellow colour (hormonal therapy); purple colour (newer drugs); blue colour (immunotherapy); grey colour (radiotherapy); * To the best of our knowledge