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O0394 Levofloxacin prophylaxis does not increase the carriage of resistant organisms - tackling early morbidity and mortality in myeloma (TEAMM) Phase III study: assessing the benefits of antibiotic prophylaxis and its effect on carriage of resistant organisms in 977 patients

Timothy David Planche*[1], Gulnaz Iqbal[2], Mark Drayson[7], Irene Monahan[1], Jill Wood[2], Kerry Raynes[2], Peter M. Hawkey[4], Guy Pratt[5], Kwee Yong[6], Janet Dunn[2], Stella Bowcock[3]

[1]St George's University of London, Institute of Infection and Immunity, London, United Kingdom, [2]University of Warwick, Warwick Clinical Trial Unit, Coventry, United Kingdom, [3]king's College Hospital NHS Trust, Haematology, London, United Kingdom, [4]University of Birmingham, Institute of Microbiology and Infection, Birmingham, United Kingdom, [5]University Hospital Birmingham NHS Trust, Haematology, Birmingham, United Kingdom, [6]University College London, Department of Haematology, UCL Cancer Institute, London, United Kingdom, [7]University of Birmingham, Institute of Immunology and Immunotherapy, Birmingham, United Kingdom

Background: Although antibiotic prophylaxis benefits some groups of patients with cancer, concerns about the selection of resistant bacteria and the development of *Clostridium difficile* infection have led to calls for the reduction in prolonged use of antibiotic prophylaxis, particularly quinolones. However, fewer hospital admissions and less use of broad-spectrum antibiotics, could paradoxically reduce risks of antibiotic resistance in patients taking prophylaxis. As a part of the Tackling Early Morbidity and Mortality in Myeloma trial (TEAMM) study, a multi-centre, phase III, randomised, placebo-controlled trial of levofloxacin prophylaxis in myeloma we prospectively studied risk factors and rates of carriage of resistant bacteria and *C. difficile*.

Materials/methods: Patients with newly diagnosed myeloma were randomised to receive levofloxacin or placebo once daily for 12 weeks. Patients were permitted to continue other routine prophylaxis with sulfamethoxazole-trimethoprim (SMZ-TMP) or acyclovir. Faecal and throat samples were taken monthly for 16 weeks to isolate carriage of *C. difficile*, MRSA and faecal ESBL-positive enterobacteraciae (ESBLEnt). We collected data on carriage, antibiotic therapy, hospital admissions, demographics and myeloma status. Comparisons were made between patients on levofloxacin and/or SMZ-TMP with those taking no antibiotics.

Results: 977 patients were recruited from 92 UK centres and around 60% of patients were not hospitalised during the study. The primary endpoint of febrile episodes and death showed a significant benefit for the use of levofloxacin with 134 events (27%) in 488 placebo patients versus 95 (19%) in 489 levofloxacin patients; p=0.002. The number of deaths by 12 weeks was significantly lower in the levofloxacin group (8 vs 22 p=0.01). There was no significant difference between the 2 arms for acquisition of carriage of *C. difficile*, MRSA and ESBLEnt (Table). SMZ-TMP (315 patients) significantly reduced the number of febrile episodes and SMZ-TMP in combination with levofloxacin had a significantly lower carriage rate of ESBLEnt than placebo 6% vs 12 % (0=0.04). Risk factors for acquisition of carriage are examined.

Conclusions: Prophylactic use of 12 weeks levofloxacin did not increase the risk of acquisition of carriage of resistant bacteria in patients with myeloma and in combination with sulfamethoxazole-trimethoprim was associated with reduced carriage of ESBLEnt.

Organism	Levofloxacin			Placebo			Total		
	C-diff	ESBL	MRSA	*C-diff*	ESBL	MRSA	*C-diff*	ESBL	MRSA
	n	n	n	n	n	n	n	n	n
Present at baseline	1	29	5	5	46	9	6	75	14
Week 4	4	9	0	3	18*	4	7	27	4
Week 8	0	7	1	2	13	1	2	20	2
Week 12	3	8	1	2	13	2	5	21	3
Week 16	4	13	2	1	7	0	5	20	2
Total new acquisitions (2595 stool, 2933 nasal samples	11	37	4	8	51	7	19	88	11