



**Figure 1. Immunohistochemical analysis of MDR1/P-gp and MRP-1 protein expression.** Representative melanoma specimens showing strongly positive (4+3) MDR1/P-gp (A) and MRP-1 (B) staining (4+3). Images (C) and (D) show specimens which were negative for MDR1/P-gp and MRP-1 staining, respectively. Image (E) represents negative control (scale bar = 100  $\mu$ m in all images; original magnifications of all photomicrographs  $\times$ 40).

**Table 1.** Clinicopathological features of patients studied for MDR1/P-gp and MRP-1 expression in melanoma primary and metastatic specimens

<b>Characteristics</b>	<b>Primary (%)</b>	<b>Metastatic (%)</b>
<b>Age (yr.)</b>		
<59	45.6 (42/92)	54.8 (23/42)
≥59	54.3 (50/92)	45.2 (19/42)
<b>Gender</b>		
Male	32.6 (30/92)	50.0 (21/42)
Female	67.4 (62/92)	50.0 (21/42)
<b>Lymph node spread</b>		
Negative	92.4 (85/92)	28.6 (12/42)
Positive	7.6 (7/92)	71.4 (30/42)
<b>Clark's</b>		
I	1.08 (1/92)	97.6 (41/42)
II	10.9 (10/92)	0 (0/42)
III	32.3 (30/92)	0 (0/42)
IV	22.8 (21/92)	0 (0/42)
V	6.5 (6/92)	2.4 (1/42)
Unknown	26.1 (24/92)	0 (0/42)
<b>Breslow Thickness</b>		
<1 mm	31.5 (29/92)	2.4 (1/42)
1 – 2 mm	18.5 (17/92)	2.4 (1/42)
2.1 – 4 mm	10.9 (10/92)	0 (0/42)
> 4 mm	21.7 (20/92)	4.8 (2/42)
Unknown	17.4 (16/92)	90.5 (38/42)
<b>Relapse</b>		
Relapse ≤5 yrs.	25.0 (23/92)	19.0 (8/42)
Did not Relapse ≤5 yrs.	14.1 (13/92)	7.1 (3/42)
Unknown	60.9 (56/92)	73.8 (31/42)

**Table 2(A).** Comparison of MDR1/P-gp and MRP-1 co-expression in all melanoma specimens analysed

<b>Drug Efflux Pump</b>	<b>% Cases</b>
MRP1 <sup>+</sup> & MDR1/P-gp <sup>+</sup>	44.0 (59/134)
MRP1 <sup>-</sup> & MDR1/P-gp <sup>+</sup>	13.4 (18/134)
MRP1 <sup>+</sup> & MDR1/P-gp <sup>-</sup>	23.1 (31/134)
MRP1 <sup>-</sup> & MDR1/P-gp <sup>-</sup>	19.4 (26/134)

**Table 2(B).** Comparison of MDR1/P-gp and MRP-1 co-expression in the primary melanoma specimens only

<b>Drug Efflux Pump</b>	<b>% Cases</b>
MRP1 <sup>+</sup> & MDR1/P-gp <sup>+</sup>	33.7 (31/92)
MRP1 <sup>-</sup> & MDR1/P-gp <sup>+</sup>	16.3 (15/92)
MRP1 <sup>+</sup> & MDR1/P-gp <sup>-</sup>	22.8 (21/92)
MRP1 <sup>-</sup> & MDR1/P-gp <sup>-</sup>	27.2 (25/92)

**Table 2(C).** Comparison of MDR1/P-gp and MRP-1 co-expression in the metastatic melanoma specimens only

<b>Drug Efflux Pump</b>	<b>% Cases</b>
MRP1 <sup>+</sup> & MDR1/P-gp <sup>+</sup>	66.7 (28/42)
MRP1 <sup>-</sup> & MDR1/P-gp <sup>+</sup>	7.1 (3/42)
MRP1 <sup>+</sup> & MDR1/P-gp <sup>-</sup>	23.8 (10/42)
MRP1 <sup>-</sup> & MDR1/P-gp <sup>-</sup>	2.4 (1/42)

**Table 3.** Correlation between expression of MDR P-gp and MRP-1 protein in primary *versus* metastatic specimens

<b>Tumour Site</b>	<b>No. of cases</b>	<b>MDR P-gp (%)</b>	<b>P</b>	<b>No. of cases</b>	<b>MRP-1 (%)</b>	<b>P</b>
Primary	46/92	50	0.010*	52/92	56.5	P<0.000*
Metastasis	31/42	73.8		38/42	90.5	

P values from  $X^2$  analyses; \* indicates significant parameter.

**Table 4.** Correlation between clinicopathological factors and expression of MDR P-gp and MRP-1 protein in all melanoma specimens analysed

<b>Characteristics</b>	<b>No. of cases</b>	<b>MDR P-gp (%)</b>	<b>P</b>	<b>No. of cases</b>	<b>MRP-1 (%)</b>	<b>P</b>
<b>Age (yr.)</b>						
<59	34/65	52.3	0.241	43/65	66.2	0.809
≥59	43/69	62.3		47/69	68.1	
<b>Gender</b>						
Male	30/51	58.8	0.803	39/51	76.5	0.072
Female	47/83	56.6		51/83	61.4	
<b>Lymph node spread</b>						
Negative	50/98	51.0	0.013*	57/98	58.2	<0.0005*
Positive	27/36	75.0		33/36	91.7	
<b>Clark's</b>						
II & III	20/41	48.8	0.251	19/41	46.3	0.051
IV & V	17/27	63.0		19/27	70.3	
<b>Clark's</b>						
II, III, IV	32/62	51.6	0.136	32/62	51.6	0.032*
V	5/6	83.3		6/6	100	
<b>Breslow Thickness</b>						
<1 mm	14/30	46.7	0.052	13/30	43.3	0.107
1 – 4 mm	11/28	39.3		16/28	57.1	
> 4 mm	16/22	72.7		11/22	50.0	
<b>Relapse</b>						
Relapse within 5 yrs.	17/31		0.260	18/31		0.252

P values from X<sup>2</sup> analyses; \* indicates significant parameter; Clark's score - information was available for 68/134 cases; Breslow's thickness - information was available on 80/134 cases

**Table 5.** Correlation between clinicopathological factors and expression of MDR P-gp and MRP-1 protein in primary tumours only

<b>Characteristics</b>	<b>No. of cases</b>	<b>MDR P-gp (%)</b>	<b>P</b>	<b>No. of cases</b>	<b>MRP-1 (%)</b>	<b>P</b>
<b>Age (yr.)</b>						
<59	19/42	45.2	0.402	22/42	52.4	0.463
≥59	27/50	54.0		30/50	60.0	
<b>Gender</b>						
Male	14/30	46.7	0.656	21/30	70.0	0.070
Female	32/62	51.6		31/62	50.0	
<b>Lymph node spread</b>						
Negative	40/85	47.1	0.049*	46/85	54.1	0.105
Positive	6/7	85.7		6/7	85.7	
<b>Clark's</b>						
II & III	20/41	48.8	0.251	19/41	46.3	0.051
IV & V	17/27	63.0		19/27	70.3	
<b>Clark's</b>						
II, III, IV	32/62	51.6	0.136	32/62	51.6	0.023*
V	5/6	83.3		6/6	100.0	
<b>Breslow Thickness</b>						
<1 mm	14/29	48.3	0.056	12/29	41.4	0.139
1 – 4 mm	11/27	40.7		15/27	55.6	
> 4 mm	15/20	75.0		14/20	70.0	
<b>Relapse</b>						
Relapse within 5 yrs.	11/23	47.8	0.587	10/23	43.5	0.137

P values from  $X^2$  analyses; \* indicates significant parameter; Clark's score - information was available for 68/92 cases; Breslow's thickness - information was available on 76/92 cases; relapse information available on 36 cases