Summary of laboratory test findings

After dosing there were decreases in haemoglobin, total white blood cells and lymphocytes across the dose range but with no clear dose relationship. There were also decreases in neutrophils with a trend for a dose effect and decreases in platelets which were dose-related. Increases in transaminases were seen, which were most frequent and most marked at doses of 6 x 10^{12} viral particles (vp) and above. The same trend was seen for decreases in albumin. Increases in bilirubin and alkaline phosphatase showed no pattern and increases in creatinine were infrequent. The maximum decrease from baseline for albumin-corrected calcium values in Phase I showed no difference between dose groups. Increases in activated partial thromboplastin time were seen but with no apparent dose relationship. The maximum changes from baseline are shown in the Table 1.

Table 1: Maximum Change from Baseline for Key Laboratory Parameters (Safety Population)

Median (Range)	**Dose Level Assigned (vp)**			
	<1 x 10^{12} N=6	**1 to 3 x 10^{12} N=26**	**>3 x 10^{12} N=29**	**All Doses N=61**
Neutrophils (x10^9/L)	-2.285 (-4.06, -1.47)	-2.080 (-3.77, -0.30)	-2.900 (-6.14, -0.49)	-2.500 (-6.14, -0.30)
Platelets (x10^9/L)	-42.0 (-91, -7)	-94.0 (-249, 5)	-111.0 (-260, -41)	-99.0 (-260, 5)
ALT (U/L)	2.0 (-22, 76)	15.0 (2, 154)	34.0 (-1, 2599)	16.0 (-22, 2599)
AST (U/L)	3.5 (-39, 126)	18.0 (0, 205)	44.4 (-14, 1233)	23.0 (-39, 1233)
Creatinine (µmol/L)	3.1 (-2, 20)	17.2 (-9, 261)	18.0 (-11, 59)	15.9 (-11, 261)
aPTT	9.55 (2.6, 46.0)	17.65 (0.6, 166.8)	11.10 (-13.9, 55.8)	14.50 (-13.9, 166.8)
Abbreviations: ALT=alanine aminotransferase; aPTT=activated partial thrombosplastin time; AST=aspartate aminotransferase; vp=viral particles. Period from time of first dose to end of safety follow-up				

The number of subjects showing two or more Common Terminology Criteria for Adverse Events (CTCAE) grade shifts during treatment for key laboratory parameters was summarised. Decreasing shifts of two or more CTCAE grades were seen in subjects for haemoglobin, total white blood cells and lymphocytes across the dose range with no clear dose relationship. There was a trend for a slight increase in the proportion of subjects with falls in neutrophils of two or more CTCAE grades with increasing dose but a marked increase in the proportion of subjects with decreases in platelets at doses above 3 x10^{12} vp. CTCAE grades shifts of two or more were more common at doses above 3 x 10^{12} vp. Alkaline phosphatase and total bilirubin increasing shifts were seen in a small number of subjects across the dose range. Only one subject had an increasing shift in creatinine of two or more CTCAE grades after the 3 x 10^{12} vp dose. Decreasing shifts in albumin were also seen across the dose range, but were more common at the higher doses. No subjects had increasing corrected calcium shifts of two or more CTCAE grades.

No subjects had increasing international normalised ratio shifts of two or more CTCAE grades. Activated partial thromboplastin time increasing shifts were seen in a small number of subjects across the dose range. The number of subjects with two or more CTCAE grade shifts is summarised in Table 2

Table 2
Laboratory Results - Subjects with Shifts of at Least Two CTCAE Grades in Laboratory Parameters During Treatment Period
Safety Analysis Set

Laboratory Parameter	Initial Dose Level Assigned: < 1 x 10^12 vp (N = 6) s/n (%)	1 - 3 x 10^12 vp (N = 26) s/n (%)	> 3 x 10^12 vp (N = 29) s/n (%)	All dosing groups (N = 61) s/n (%)
Haemoglobin - decrease	0/6	5/26 (19.2%)	1/29 (3.4%)	6/61 (9.8%)
Leukocytes - decrease	1/6 (16.7%)	10/26 (38.5%)	8/29 (27.6%)	19/61 (31.1%)
Lymphocytes - decrease	3/6 (50.0%)	15/26 (57.7%)	18/29 (62.1%)	36/61 (59.0%)
Neutrophils - decrease	1/6 (16.7%)	6/26 (23.1%)	10/29 (34.5%)	17/61 (27.9%)
Platelets - decrease	0/6	2/26 (7.7%)	9/29 (31.0%)	11/61 (18.0%)
Activated Partial Thromboplastin Time - increase	1/6 (16.7%)	9/21 (42.9%)	4/22 (18.2%)	14/49 (28.6%)
Prothrombin Intl. Normalized Ratio - increase	0/6	0/26	0/29	0/61
Alanine Aminotransferase - increase	0/6	1/26 (3.8%)	7/29 (24.1%)	8/61 (13.1%)
Albumin - decrease	1/6 (16.7%)	3/26 (11.5%)	8/29 (27.6%)	12/61 (19.7%)
Alkaline Phosphatase - increase	2/6 (33.3%)	3/26 (11.5%)	2/29 (6.9%)	7/61 (11.5%)

vp = viral particles
Treatment period = From first dose till the earlier of: date of last dose + 28 days; date of progression for date of progression occurring after last dose; start of subsequent cancer treatment for cancer treatments starting after last dose.
N = number of subjects in the group, n = number of subjects in the group with an evaluable assessment during the treatment period
s = number of subjects with a shift of at least two CTCAE grades in laboratory parameter during the treatment period
Percentages are calculated with respect to the number of subjects in the group with an evaluable assessment during the treatment period
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Table 15
Laboratory Results - Subjects with Shifts of at Least Two CTCAE Grades in Laboratory Parameters During Treatment Period
Safety Analysis Set

Laboratory Parameter	Initial Dose Level Assigned: < 1 x 10^12 vp (N = 6) s/n (%)	1 - 3 x 10^12 vp (N = 26) s/n (%)	> 3 x 10^12 vp (N = 29) s/n (%)	All dosing groups (N = 61) s/n (%)
Aspartate Aminotransferase - increase	1/6 (16.7%)	4/26 (15.4%)	9/29 (31.0%)	14/61 (23.0%)
Creatinine - increase	0/6	1/26 (3.8%)	0/29	1/61 (1.6%)
Total Bilirubin - increase	1/6 (16.7%)	2/26 (7.7%)	3/29 (10.3%)	6/61 (9.8%)

vp = viral particles
Treatment period = From first dose till the earlier of: date of last dose + 28 days; date of progression for date of progression occurring after last dose; start of subsequent cancer treatment for cancer treatments starting after last dose.
N = number of subjects in the group, n = number of subjects in the group with an evaluable assessment during the treatment period
s = number of subjects with a shift of at least two CTCAE grades in laboratory parameter during the treatment period
Percentages are calculated with respect to the number of subjects in the group with an evaluable assessment during the treatment period

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Table 15
Laboratory Results - Subjects with Shifts of at Least Two CTCAE Grades in Laboratory Parameters During Treatment Period
Safety Analysis Set - ColoAd1-1001 Phase 1a

	Initial Dose Level Assigned			
Laboratory Parameter	< 1 x 10^12 vp (N = 6) s/n (%)	1 - 3 x 10^12 vp (N = 9) s/n (%)	> 3 x 10^12 vp (N = 22) s/n (%)	All dosing groups (N = 37) s/n (%)
Calcium Corrected - decrease	0/6	0/9	0/12	0/27

vp = viral particles
Treatment period = From first dose till the earlier of: date of last dose + 28 days; date of progression for date of progression occurring after last dose; start of subsequent cancer treatment for cancer treatments starting after last dose.
N = number of subjects in the group, n = number of subjects in the group with an evaluable assessment during the treatment period
s = number of subjects with a shift of at least two CTCAE grades in laboratory parameter during the treatment period
Percentages are calculated with respect to the number of subjects in the group with an evaluable assessment during the treatment period

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