

# Preliminary results of a Phase 1 study of intravenous administration of GL-ONC1 Vaccinia virus in patients with advanced solid cancer with real time imaging. 534P

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## BACKGROUND

•GLV-1h68/GL-ONC1 is a genetically engineered live vaccinia virus attenuated by insertion of the *ruc-gfp* (a luciferase and green fluorescent protein fusion gene), beta-galactosidase (*LacZ*) and beta-glucuronidase (*gusA*) reporter genes into the *F14.5L*, *J2R* (thymidine kinase) and *A56R* (hemagglutinin) loci respectively.

### Strategy of mechanism:

1. Replicates only within the cytoplasm of the cancer cells.
2. Deletion of thymidine gene leads to dependence of virus on cellular thymidine kinase expression, which is constitutively expressed at high levels in the majority of cancer cells.
3. Direct infection of cancer cells results in cell lysis and death.
4. Adaptive and innate immune response are harnessed to fight cancer.
5. Diagnostic proteins are produced so tumour regression can be supervised.

## METHOD

- See Figure 3.
- Green-fluorescent protein (GFP) imaging was performed at baseline and during each cycle on patients with superficial or mucosal lesions.
- Endpoints were safety, tolerability, viral replication, tumour delivery, neutralizing antibody development, anti-tumour activity and recommendation of dose/schedule for future trials.

## ACKNOWLEDGEMENTS

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## REFERENCES

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## RESULTS

- Seventeen patients have been treated with no dose limiting toxicities (DLT) observed.
- Adverse events see Table 2. One patient was diagnosed with radiological changes in his spleen and an arterial embolism which we believe was caused by his underlying disease and not drug related.
- The rash comprising of vaccinia pustules appeared in two patients in cycle 1 during the first week and resolved without treatment at the end of cycle 1. It was positive for GL-ONC1 viral plaque assay (VPA) and GFP imaging. See Figure 2.
- VPA of blood, urine, stool and sputum were negative for viral shedding in all except one patient. See Table 3.
- Best response was stable disease by RECIST observed in five patients for 3 to 6 months but one patient received 8 months of treatment.

## CONCLUSION

- GL-ONC1 is well tolerated with minimal toxicity and preliminary evidence of anticancer activity.

Figure 1. Loci of inserted genes

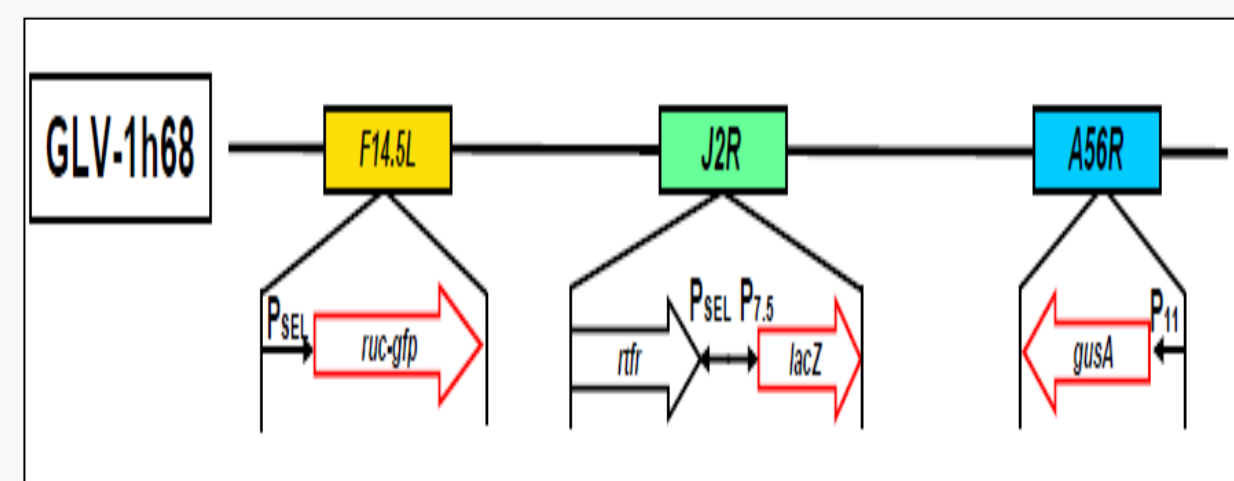


Table 1. Patient characteristics

Age, years		
Median	57	
Range	39-71	
Gender	N	%
Male	13	76
Female	4	24
Tumor type		
Melanoma	6	35
Head and Neck	3	18
Parotid	2	12
Oesophagus	1	6
Thyroid	1	6
Colorectal	4	23

Figure 3. Dose escalation scheme

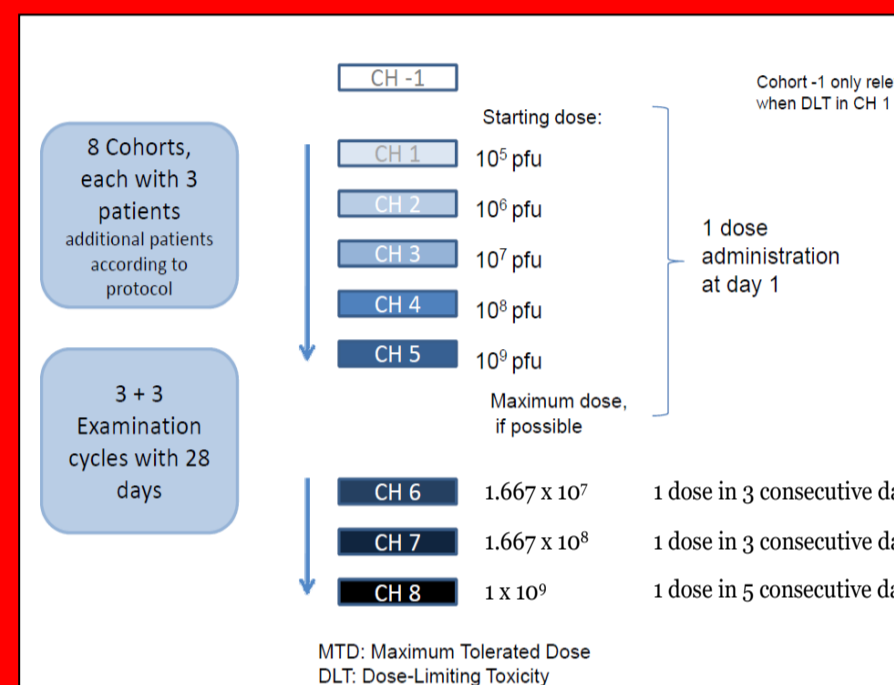


Figure 4. Pharmacokinetics

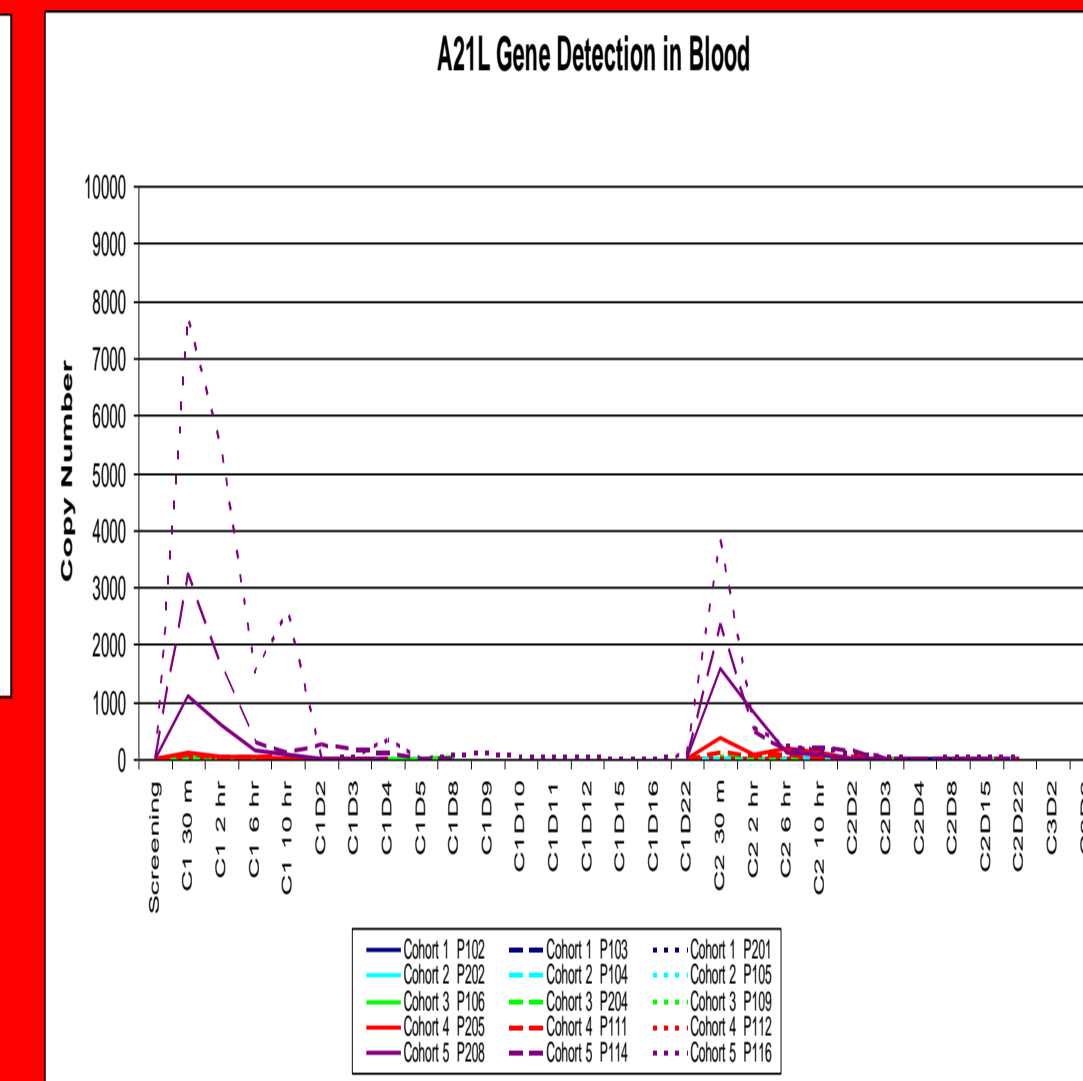


Figure 5. Vaccinia virus

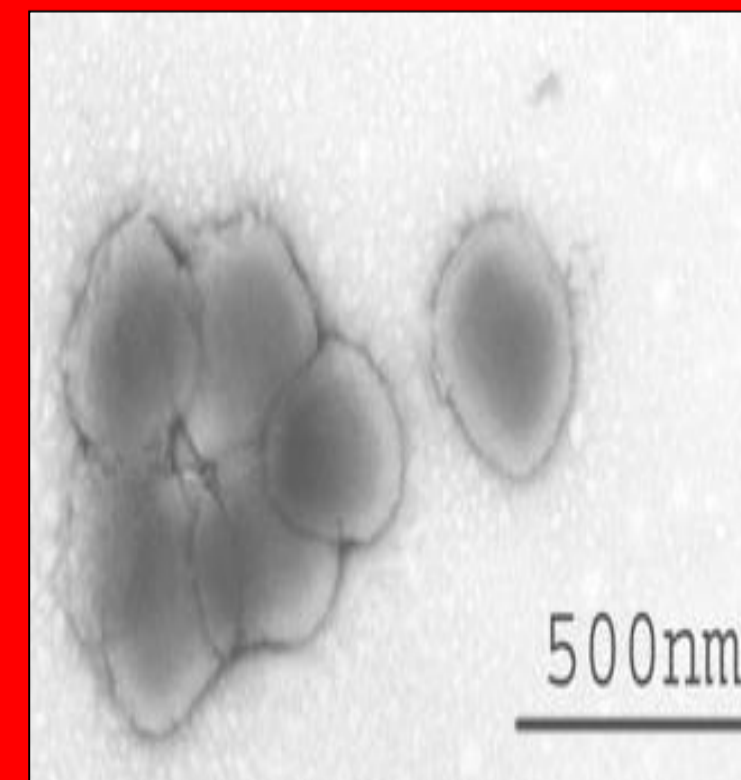


Figure 2. GFP imaging of rash

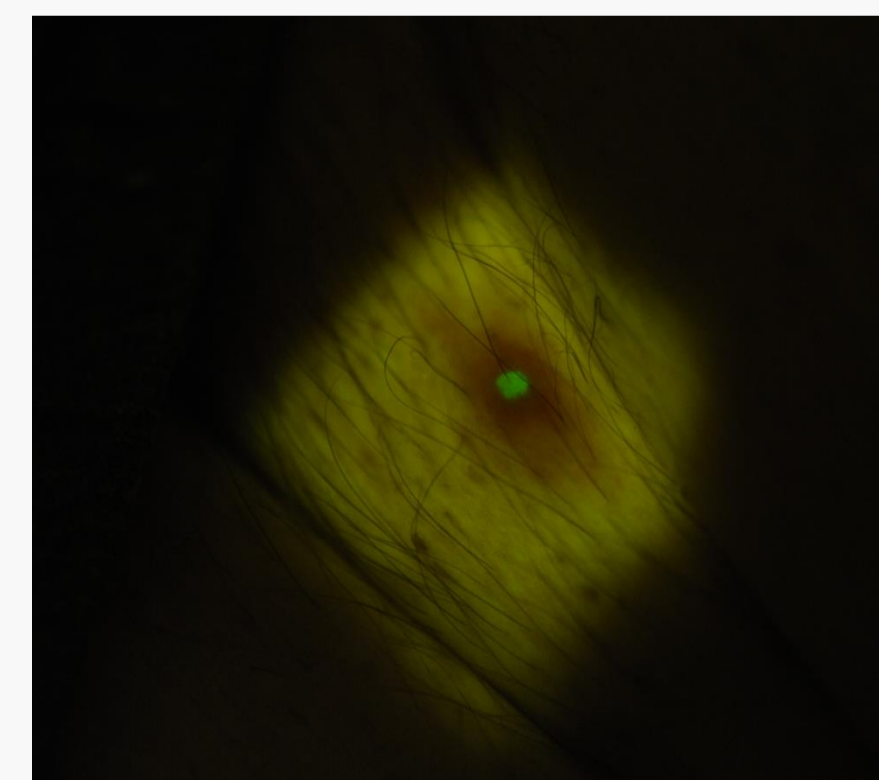


Table 2. Adverse events

	Grade 1	Grade 2
Fatigue	2	1
Fever	6	1
Oily hair/skin	1	0
Myalgia	1	1
Flu-like symptoms	2	0
Rash	1	1
Anemia	0	2
Leukopenia	0	1
Neutropenia	0	1
Leukocytosis	1	0

Figure 6. Neutralizing antibody

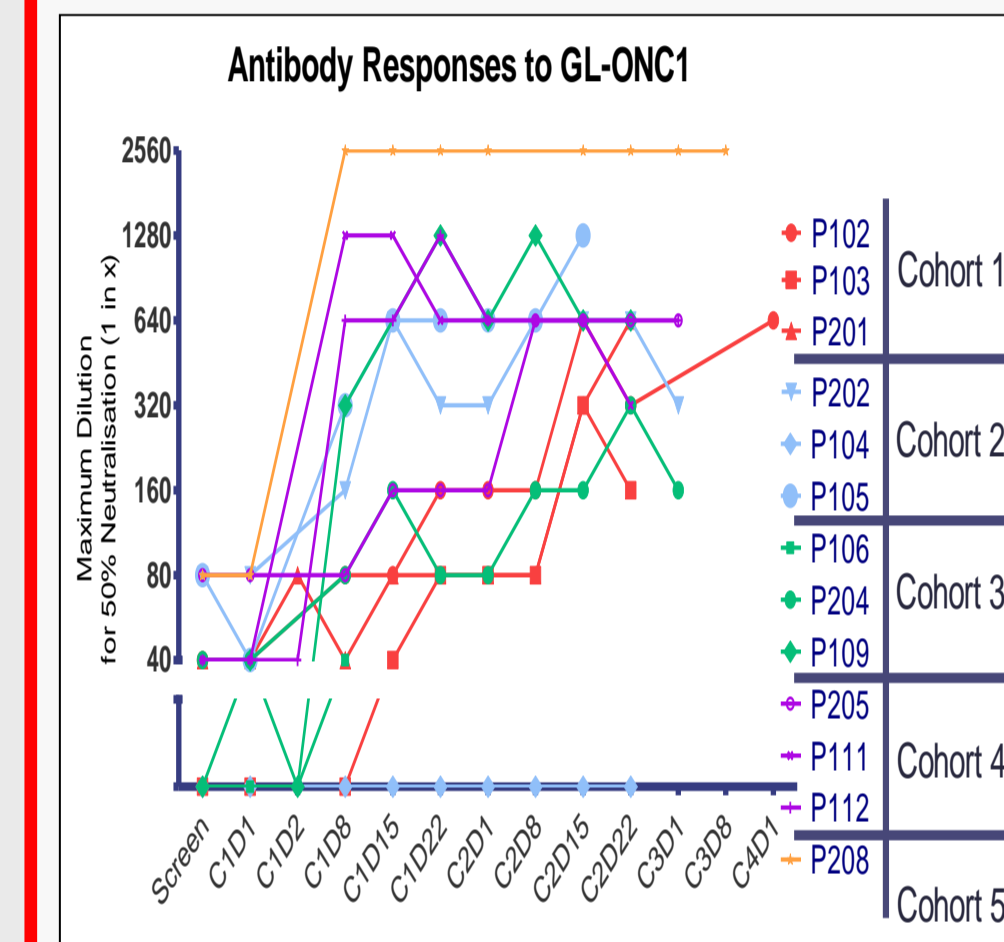


Table 3. Viral shedding (pfu) in patient 116

Day	Blood	Saliva	AS	Skin
2	1	0	1	n.a.
3	0	0	0	n.a.
4	0	37	0	n.a.
5	0	74	1	n.a.
6	n.a.	n.a.	n.a.	n.a.
7	n.a.	n.a.	n.a.	n.a.
8	0	61	0	n.a.
9	0	120	1	n.a.
10	0	15	1	n.a.
11	0	0	0	83
12	0	0	0	n.a.
13	n.a.	n.a.	n.a.	n.a.
14	n.a.	n.a.	n.a.	n.a.
15	0	0	0	n.a.
16	0	0	0	n.a.