Idelalisib in Lymphoma

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Disclosures for Stephen Ansell, MD, PhD

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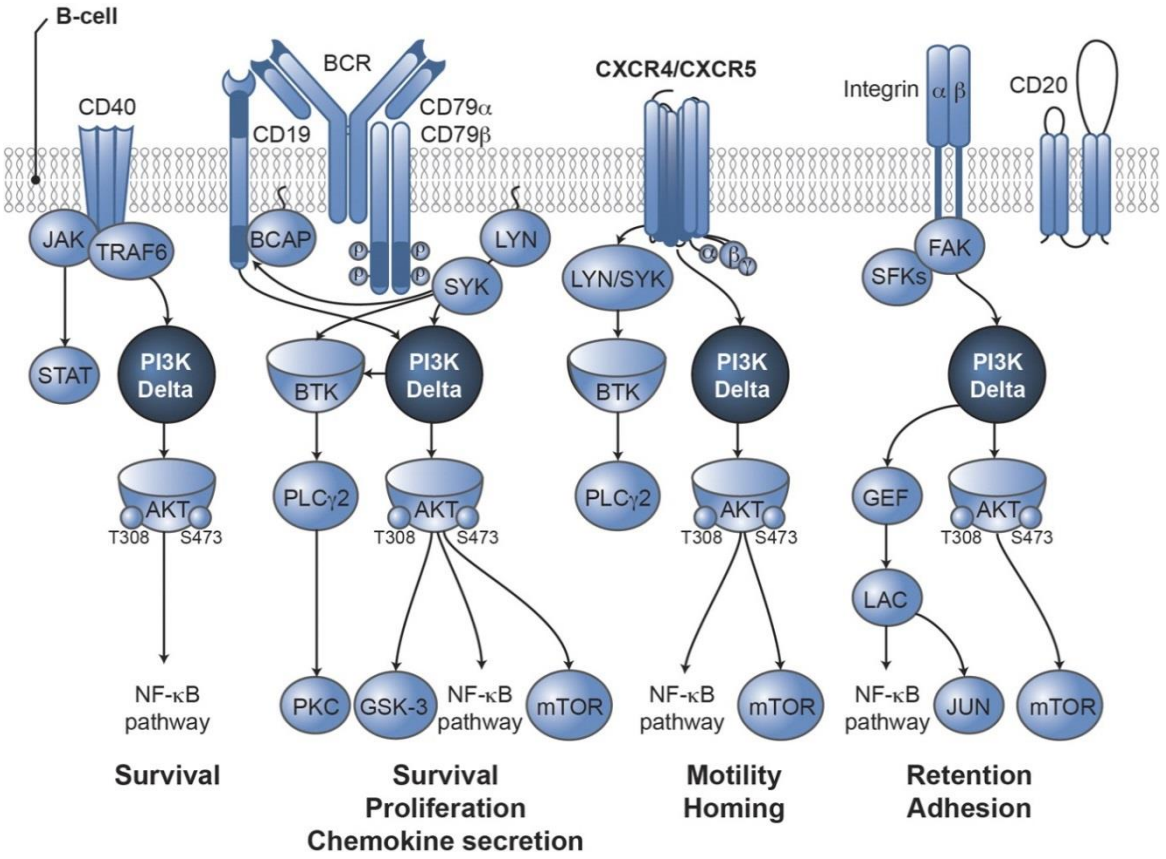
Research Support/P.I.	PI – Seattle Genetics, BMS, Affimed, Regeneron, Pfizer clinical trials
Employee	N/A
Consultant	N/A
Major Stockholder	N/A
Speakers' Bureau	N/A
Scientific Advisory Board	N/A

N/A = Not Applicable (no conflicts listed)

Lessons Learned

- Targeting the pathway results in significant efficacy
- Targeting the pathway may also result in toxicities that may occur late
- Combinations are challenging – particularly in more immune competent patients.

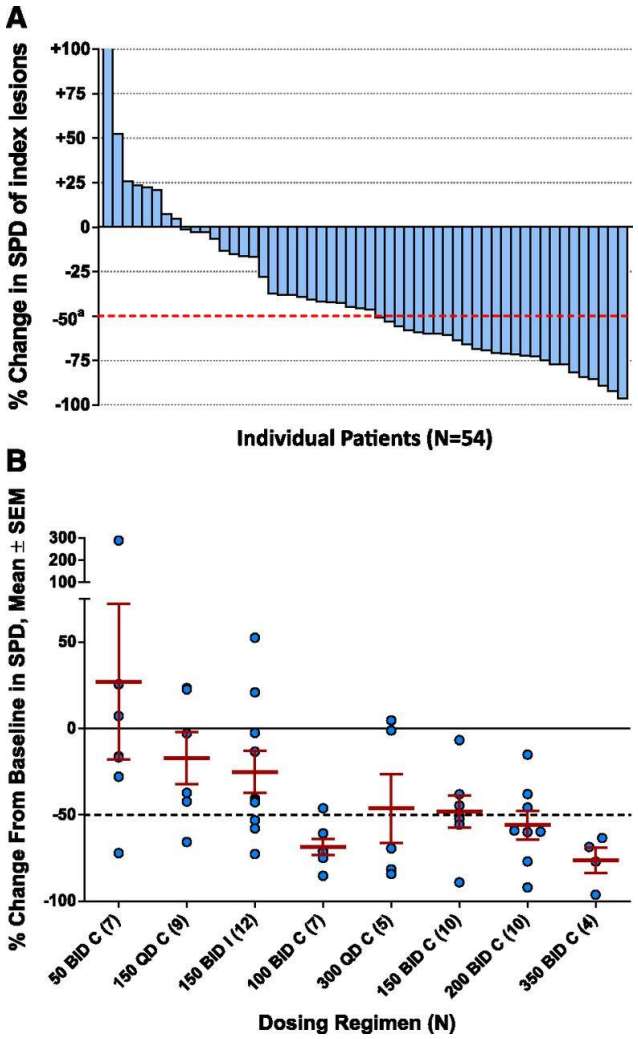
Idelalisib-induced inhibition of the PI3Kδ pathway in lymphoma.



Idelalisib is an orally bioavailable, small-molecule inhibitor of the delta isoform (p110δ) of phosphoinositide 3-kinase (PI3K)

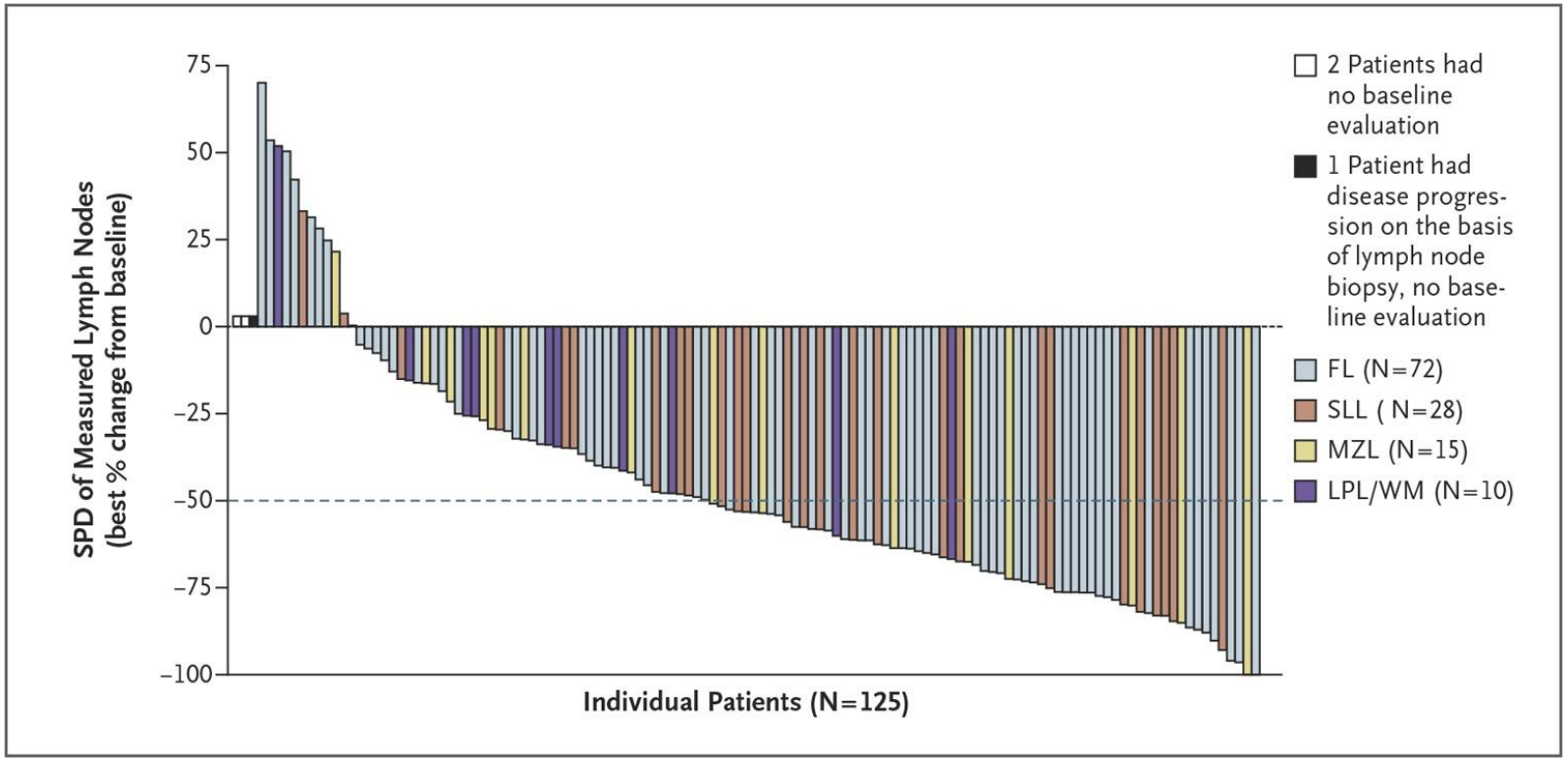
Coutré SE, et al. Leuk Lymphoma. 2015;56(10):2779-86.

Idelalisib, a selective inhibitor of PI3-kinase-δ, as therapy for previously treated indolent non-Hodgkin lymphoma – Phase 1 results



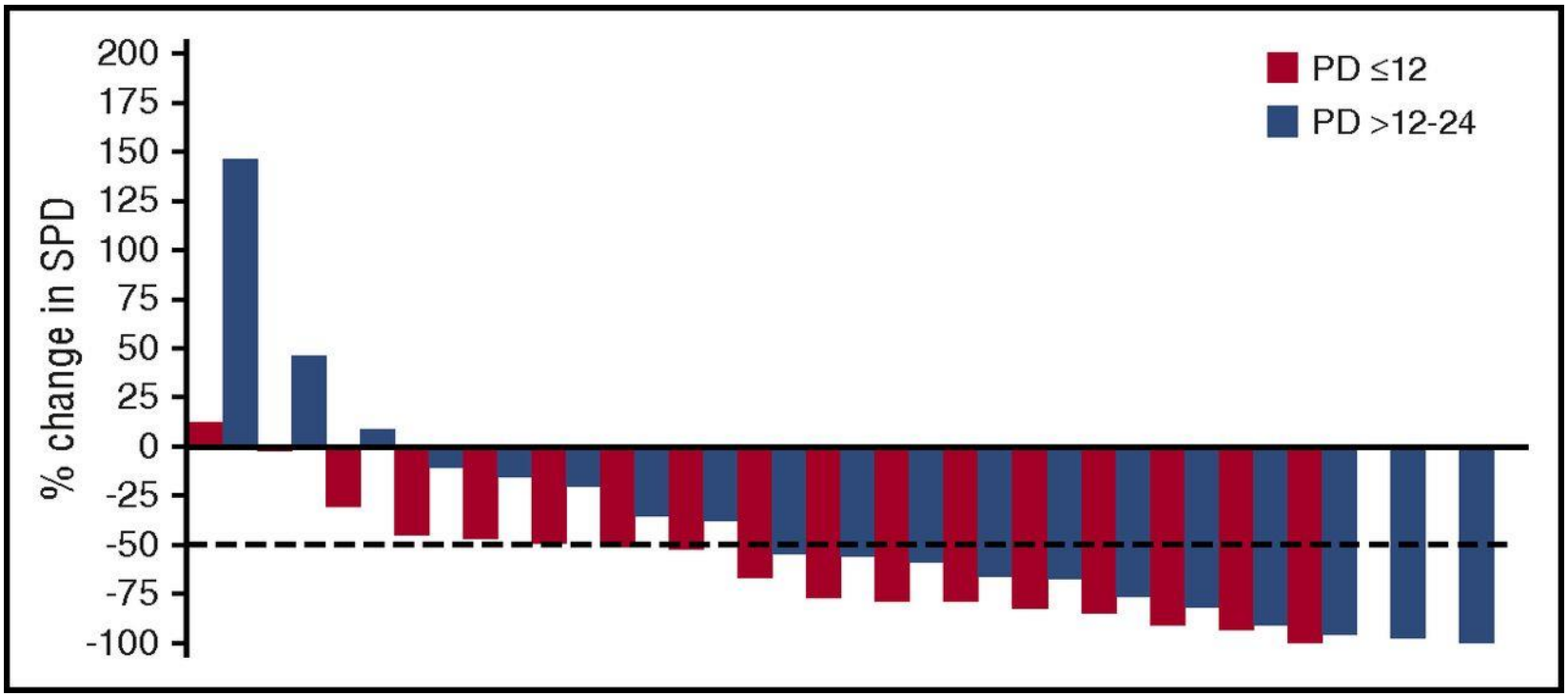
Flinn et al. Blood 2014;123:3406-3413

PI3Kδ inhibition by idelalisib in patients with relapsed indolent lymphoma – Phase 2 results



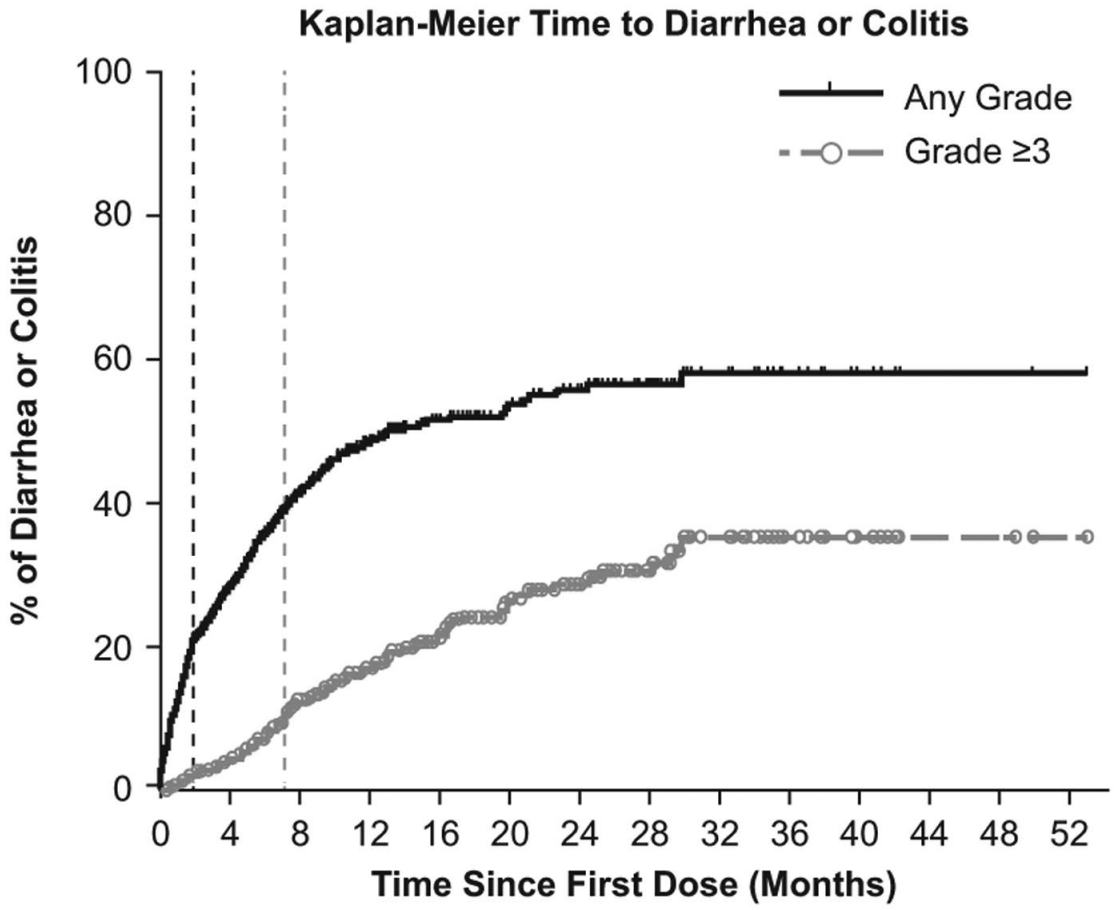
Gopal et al. N Engl J Med. 2014 Mar 13;370(11):1008-18.

Response to idelalisib therapy in Follicular Lymphoma patients who are Early Relapsers



Gopal et al. Blood 2017;129:3037-3039

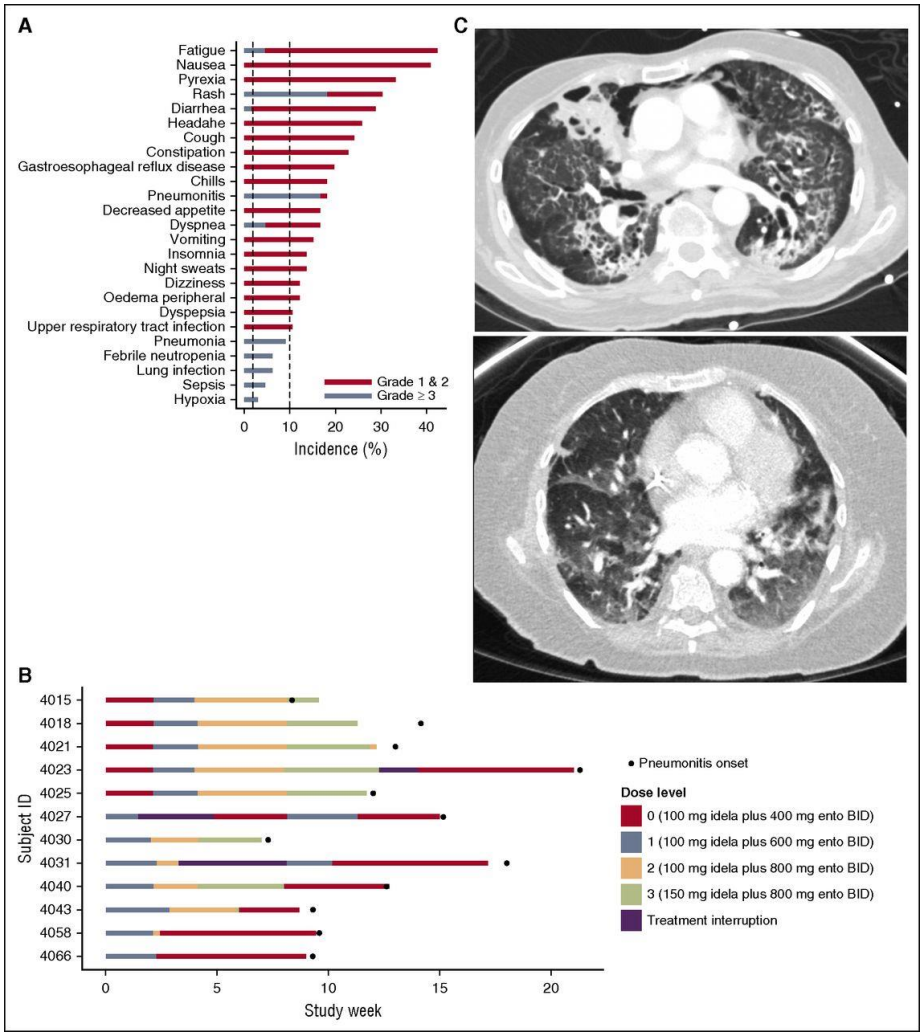
Time to onset of any grade or grade ≥ 3 diarrhea or colitis in patients treated with idelalisib



Vertical dot line represents median time to onset calculated based on all subjects with an event

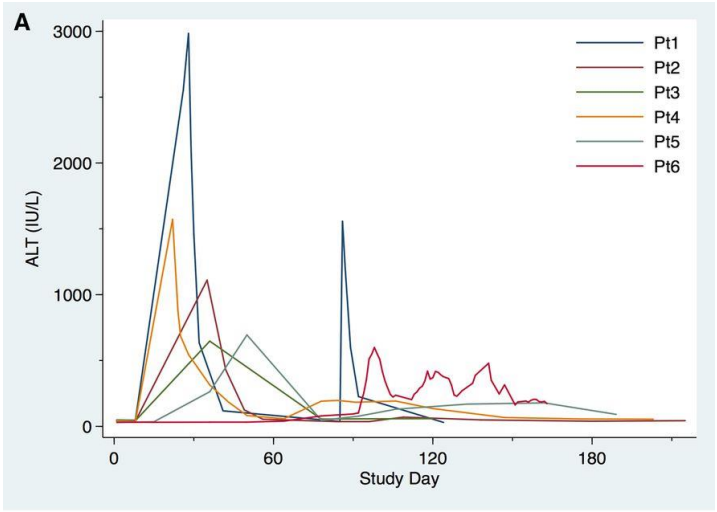
Coutré SE, et al. Leuk Lymphoma. 2015;56(10):2779-86.

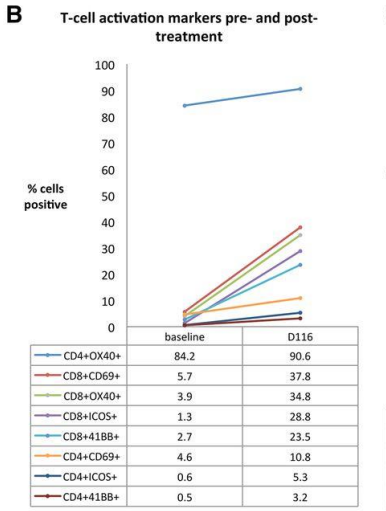
Phase 2 study of idelalisib and entospletinib: pneumonitis limits combination therapy in relapsed refractory CLL and NHL (N = 66).



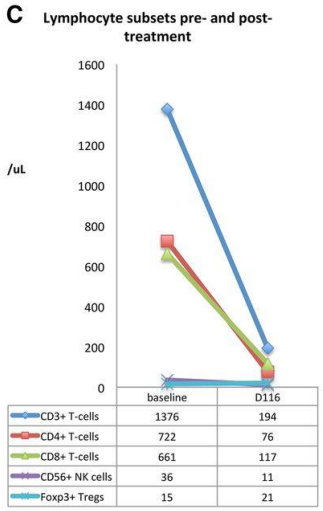
Barr et al. Blood 2016;127:2411-2415

Liver Function and immunologic changes in patients treated with rituximab, lenalidomide, and idelalisib





	baseline	D116
CD4+OX40+	84.2	90.6
CD8+CD69+	5.7	37.8
CD8+OX40+	3.9	34.8
CD8+ICOS+	1.3	28.8
CD8+41BB+	2.7	23.5
CD4+CD69+	4.6	10.8
CD4+ICOS+	0.6	5.3
CD4+41BB+	0.5	3.2



	baseline	D116
CD3+ T-cells	1376	194
CD4+ T-cells	722	76
CD8+ T-cells	661	117
CD56+ NK cells	36	11
Foxp3+ Tregs	15	21

Similar findings in the 11 patients in the Alliance for Clinical Trials in Oncology A051201 and A051202 phase 1 trials

Cheah et al. Blood 2015;125:3357-3359
Smith et al. Lancet Haematol, 2017: 4(4), e176-e182,

Conclusions

- Targeting the pathway results in significant efficacy but also affects pathways that result in toxicity
- Targeting the pathway may also result in toxicities that may occur late and ongoing follow up is important
- Combinations are challenging particularly due to immune immune activation.