

POSTER PRESENTATION

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# Phase I/II study of nivolumab with or without ipilimumab for treatment of recurrent small cell lung cancer (SCLC): CA209-032

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## Background

Treatment options for SCLC after failing platinum-based (PLT) chemotherapy (CT) are limited. Combined blockade of programmed death-1 (PD-1) and cytotoxic T-lymphocyte antigen-4 (CTLA-4) immune checkpoint pathways has anti-tumor activity with a manageable safety profile. Nivolumab is a fully human IgG4 PD-1 immune checkpoint inhibitor approved for melanoma and squamous NSCLC in the US and for melanoma in the EU and Japan. Interim efficacy and safety of nivolumab +/- ipilimumab, a CTLA-4 checkpoint inhibitor, in pretreated SCLC patients are reported.

## Methods

Patients with progressive disease (PD) after PLT first-line treatment were eligible, regardless of platinum sensitivity, tumor PD-L1 expression, or number of prior CT regimens. Patients were randomized to nivolumab 3 mg/kg IV Q2W or nivolumab+ipilimumab (1+1 mg/kg or 1+3 mg/kg) IV Q3W for 4 cycles, followed by nivolumab 3 mg/kg Q2W. Primary objective was objective response rate (ORR). Additional objectives included safety, progression-free survival (PFS), overall survival (OS), and biomarker analysis.

## Results

Of 90 patients enrolled (nivolumab, n=40; nivolumab+ipilimumab, n=50 [nivolumab 1+ipilimumab 1, n=3; nivolumab 1+ipilimumab 3, n=47]), 53% had  $\geq 2$  prior regimens. Efficacy results for evaluable patients are

shown (Table 1). 20% of patients in the nivolumab arm and 42% in the nivolumab+ipilimumab arms remain on treatment. Discontinuations due to treatment-related adverse events (TRAEs) occurred in 8% of nivolumab and 11% of nivolumab+ipilimumab patients. TRAEs (all grades) in  $\geq 10\%$  of patients included fatigue (18%), diarrhea (13%), nausea (10%), and decreased appetite (10%) with nivolumab; and diarrhea (23%), fatigue (21%), rash (21%), pruritus (19%), hypothyroidism (15%), hyperthyroidism (13%), nausea (13%), maculopapular rash (13%), and increased lipase (11%) with nivolumab 1+ipilimumab 3. Grade 3–4 TRAEs in  $\geq 5\%$  of patients occurred only in the nivolumab 1+ipilimumab 3 arm and included diarrhea (9%) and increased lipase (6%). Pneumonitis occurred in 2 patients in the nivolumab arm (grade 1–2) and 1 patient in the nivolumab 1+ipilimumab 3 arm (grade 3–4). One patient in the nivolumab 1+ipilimumab 3 arm had treatment-related myasthenia gravis with fatal outcome. Updated efficacy, safety, biomarker analysis, and case studies (responses in a patient with PLT-refractory disease and in a patient after cross-over to nivolumab/ipilimumab) will be presented.

## Conclusions

In this PD-L1 unselected SCLC population with progression after PLT-CT, nivolumab monotherapy and nivolumab+ipilimumab were generally well tolerated with manageable toxicity. Rare severe toxicities will require close follow-up. Durable responses occurred with nivolumab monotherapy and in combination with ipilimumab.

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**Table 1**

	Nivolumab (n=40)	Nivolumab + Ipilimumab (n=46) <sup>a</sup>
ORR, %	18	17
Complete response, %	0	2.2
Partial response, %	18	15
Stable disease, <sup>b</sup> %	20	37
Disease control rate, %	38	54
Progressive disease, %	53 <sup>c</sup>	37
Death prior to first response assessment, %	10	6.5 <sup>d</sup>
Not evaluable (no tumor assessment follow-up), %	0	2.2 <sup>e</sup>
Median time to objective response (months)	1.6	2.2
Median DOR, months (95% CI) Range	NR 4.1-11+	6.9 (1.5 NR) 1.5-11,1+

DOR=duration of response; NR=not reached.

<sup>a</sup>4 of 50 patients did not reach first tumor assessment at database lock.

<sup>b</sup>Of 17 patients with stage disease in the nivolumab + ipilimumab arm, 7 had confirmed partial response after database lock, resulting in updated ORR of 32.6%.

<sup>c</sup>1 patient had progressive disease in the spine, requiring surgery.

<sup>d</sup>1 patient died due to an unrelated adverse event, 1 patient died due to treatment-related myasthenia gravis, 1 patient died due to progressive disease.

<sup>e</sup>1 patient had an unrelated adverse event leading to permanent discontinuation, and had no post-baseline tumor assessment.

## Trial Registry

Clinical Trial Number: NCT01928394.

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