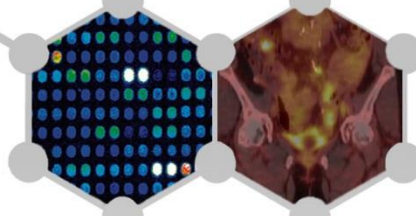

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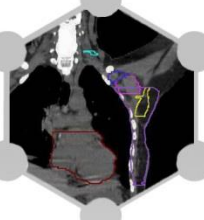

ADXS11-001 immunotherapy in squamous or non-squamous persistent/recurrent metastatic cervical cancer: Results from stage 1 [and stage 2] of the phase II GOG/NRG-0265 study

NCT01266460

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Background/Rationale

- PRmCC is a lethal disease: Median OS = 13–17 mo with access to first-line SOC, platinum-based doublet chemotherapy +/– bev[1]
  - There is no therapy following failure of first-line treatment; survival only 4–7 mo[2]
- GOG conducted >20 ph 2 studies in PRmCC from 1998–2015
  - 12-month OS rate never significantly exceeded 30%
  - Only 1 study met the predefined efficacy and safety threshold to progress to second stage of enrollment (GOG-227C)
    - Bev median OS = 7.3 months and 12-month OS = 30%
  - Limited therapies beyond first line
- ADXS11-001 immunotherapy
  - Live attenuated *Listeria monocytogenes* (*Lm*) immunotherapy bioengineered to secrete an HPV-16 E7 protein fused with a truncated fragment of listeriolysin O (tLLO)
  - Targets HPV-transformed cells, inducing antitumor T-cell immunity and breaking immune tolerance in the tumor microenvironment
- Ph II randomized trial of ADXS11-001 +/– cisplatin in Indian pts with PRmCC (0–2 prior lines of therapy) demonstrated promising activity (12-mo survival rate = 32%) and acceptable toxicity[3]
  - Activity observed across all HPV types (16, 18, 45, other)

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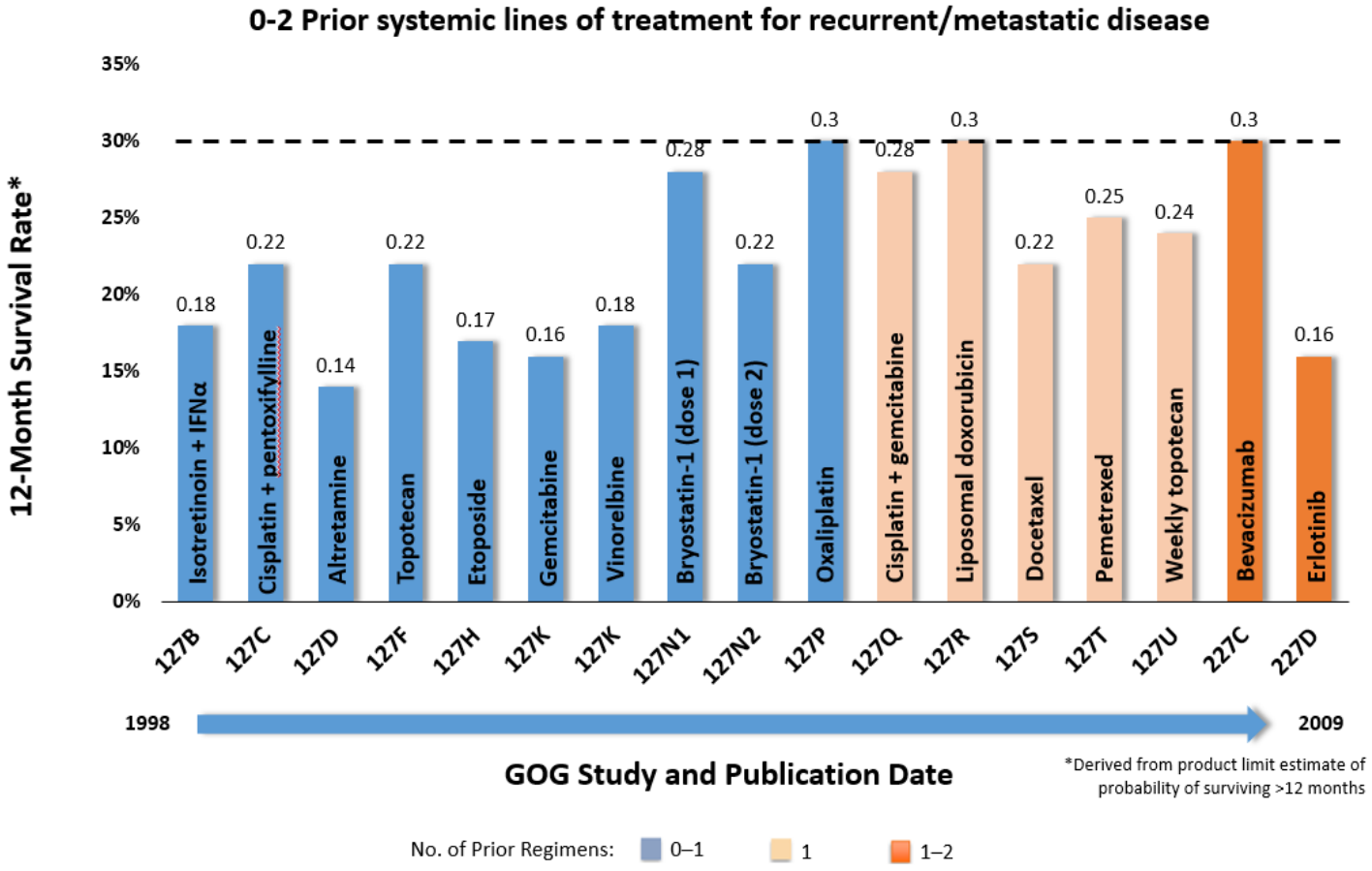
bev, bevacizumab; GOG, Gynecologic Oncology Group, now NRG Oncology; HPV, human papillomavirus; LLO, listeriolysin O; *Lm, Listeria monocytogenes*; mo, months; OS, overall survival; ph, phase; PRmCC, persistent/recurrent metastatic cervical cancer; pts, patients; SOC, standard of care.

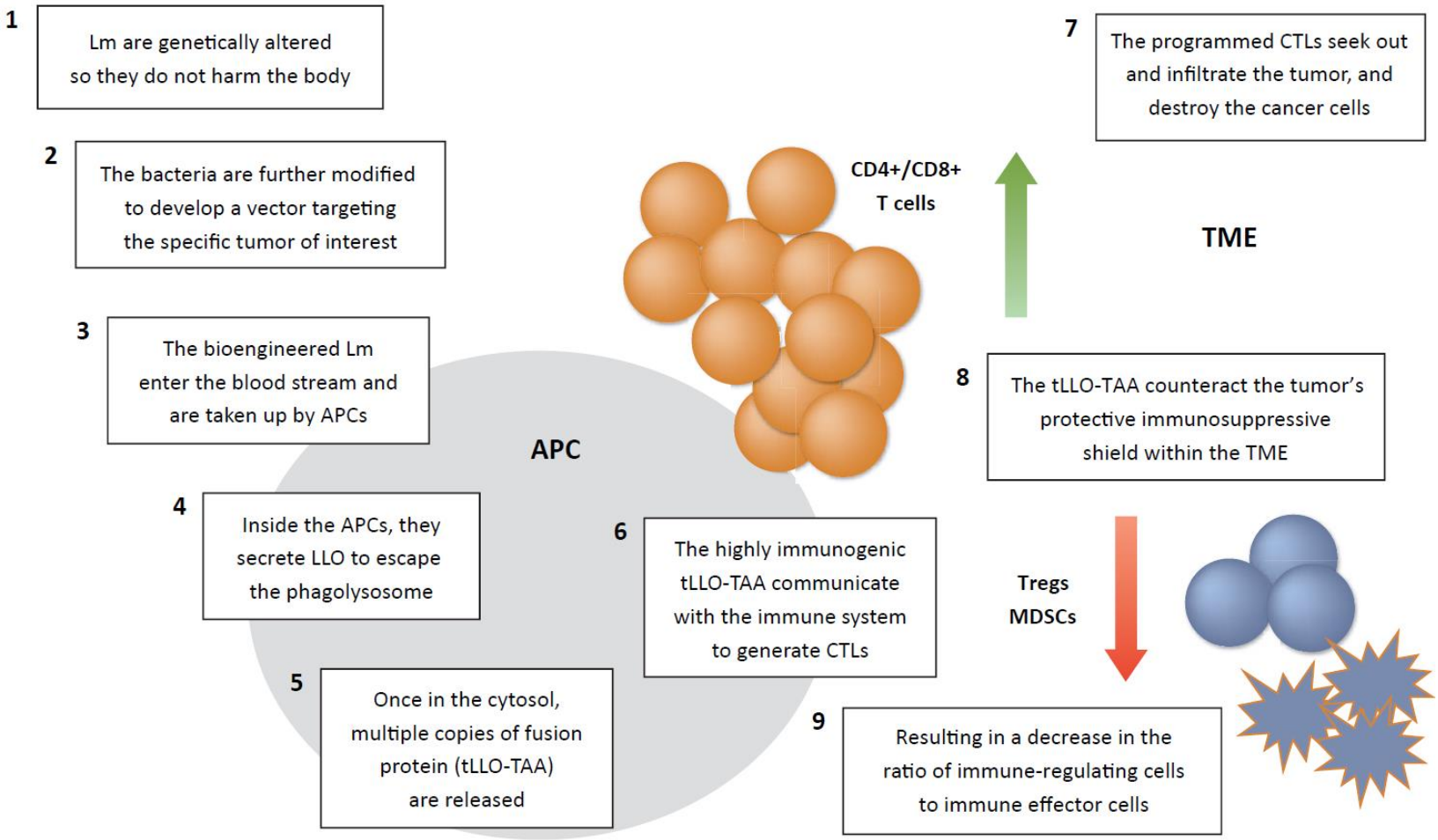
1. Tewari KS, et al. *N Engl J Med.* 2014;370(8):734-743. 2. Monk BJ, et al. *J Clin Oncol.* 2009;27(7):1069-1074.3. Basu P, et al. *J Clin Oncol.* 2014;32(suppl): abstract 5610.

12-Month Survival Rates in Pretreated PRmCC: The GOG Experience



1. Tewari KS, Monk BJ. *Curr Oncol Rep*. 2005;7(6):419-434; 2 Muggia F, et al. *Gynecol Oncol*. 2004;92(2):639-643; 3. Plaxe SC, et al. *Cancer Chemother Pharmacol.* 2002;50(2):151-154; 4. Armstrong DK, et al. *Invest New Drugs*. 2003;21(4):453-457; 5. Fracasso PM, et al. *Gynecol Oncol*. 2003;90(1):177-180; 6. Brewer CA, et al. *Gynecol Oncol*. 2006;100(2):385-388; 7. Rose P, et al. *Gynecol Oncol*. 2006;102(2):210-213; 8.Garcia AA, et al. *Am J Clin Oncol.* 2007;30(4):428-431; 9. Miller DS, et al. *Gynecol Oncol*. 2008;110(1):65-70; 10. Fiorica JV, et al. *Gynecol Oncol*. 2009;115(2):285-289; 11. Monk BJ, et al. *J Clin Oncol.* 2009;27(7):1069-1074; 12. Schilder RJ, et al. *Int J Gynecol Cancer.* 2009;19(5):929-933; 13. National Cancer Institute. Vaccine therapy in treating patients with persistent or recurrent cervical cancer. http://www.cancer.gov/about-cancer/treatment/clinical-trials/search/view?cdrid=691288. Accessed May 25, 2016.

Step-by-Step *Lm*-LLO Immunomodulation



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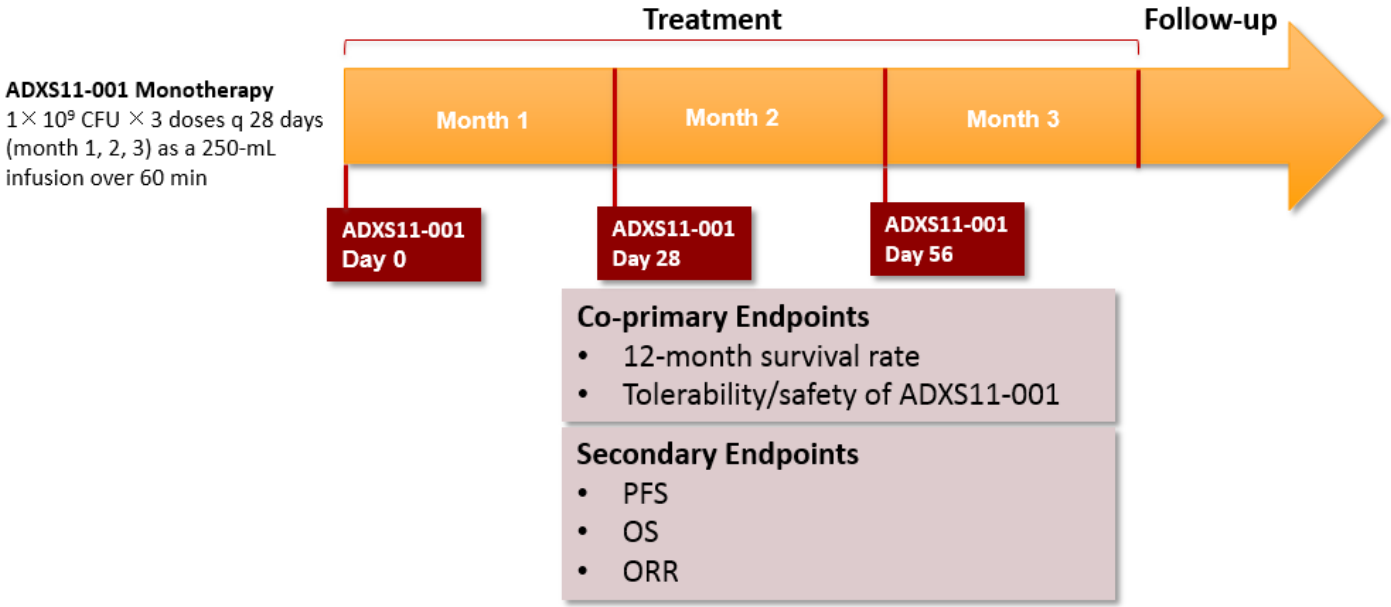
APCs, antigen-presenting cells; CD, cluster of differentiation; CTL, cytotoxic T lymphocyte; LLO, listeriolysin O; *Lm, Listeria monocytogenes*; MDSCs, myeloid-derived suppressor cells; TAA, tumor-associated antigen; tLLO, truncated LLO; TME, tumor microenvironment; Tregs, T-regulatory cells.

Krupar R, et al. Presented at the 107th Annual Meeting of the American Association for Cancer Research; April 16–20, 2016; New Orleans, LA. Abstract LB-095.

GOG/NRG-0265 Study Design and Eligibility

- N = ~63; Simon two-stage design
- ≥18 years
- Persistent/recurrent metastatic (PRmCC) squamous/non-squamous cervical cancer
- ≥1 prior line of systemic-dose therapy for PRmCC, *excluding that received as a component of primary curative treatment*
- Prior bevacizumab allowed, but not required
- GOG PS 0/1
- Measurable disease ≥1 target lesion (RECIST 1.1)



*Stage 2 amended to allow continuous (>3) dosing of ADXS11-001.

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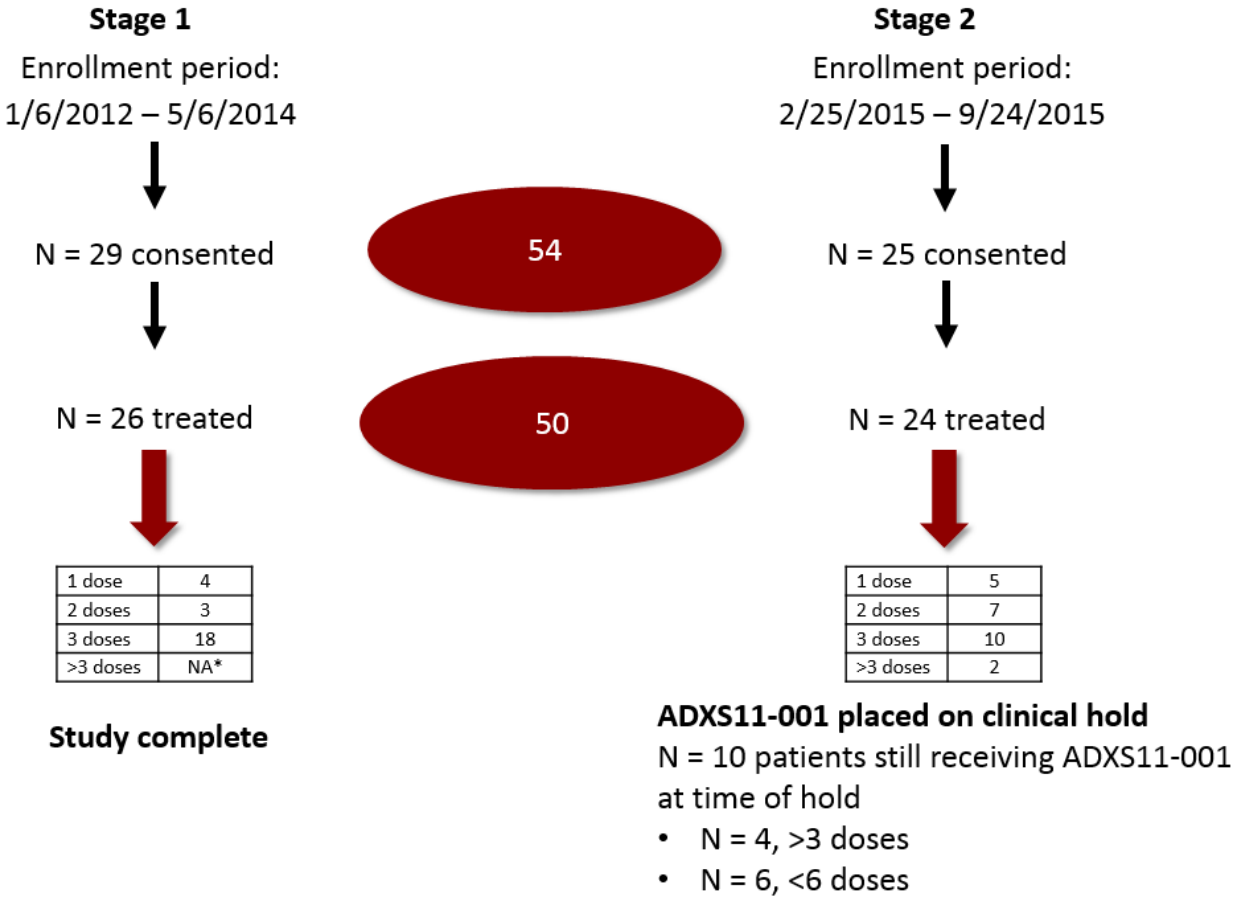
CFU, colony-forming units; ORR, objective response rate; PFS, progression-free survival; RECIST, Response Evaluation Criteria In Solid Tumors.
https://www.clinicaltrials.gov/ct2/show/NCT01266460.

CONSORT Diagram



*Maximum of 3 doses allowed on stage 1 protocol.

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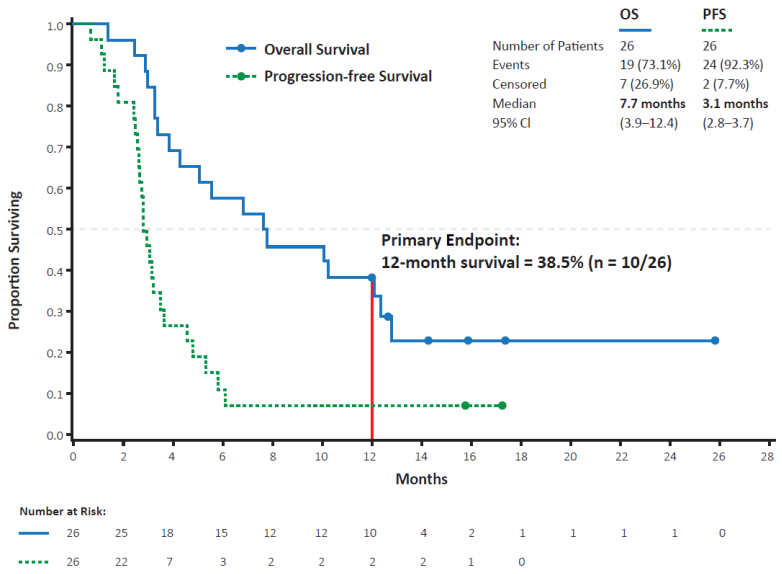
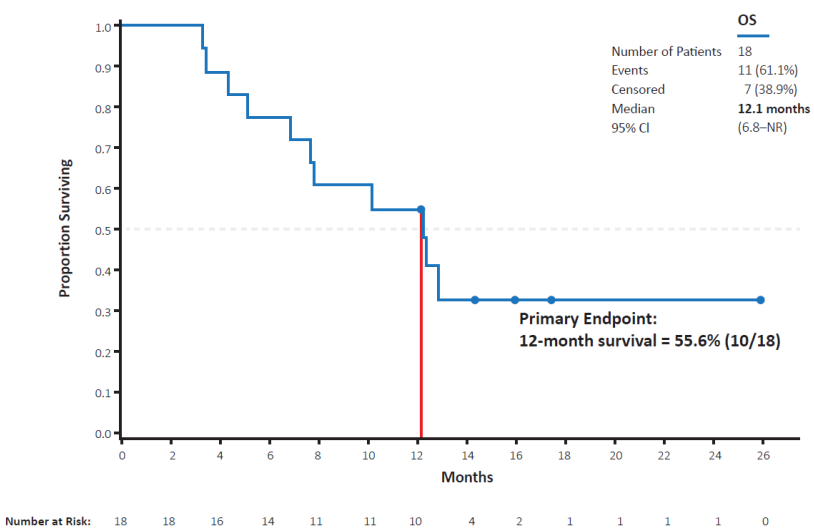
Overall Survival

STAGE 1

All patients



3 doses of ADXS11-001



STAGE 2

	All Patients (N = 24)	>3 Doses of ADXS11-001 (N = 12)
6-month OS	42% (n = 10/24)	67% (n = 8/12)
Median OS (95% CI)	4.8 months (3.8–NR)	NR (3.5–NR)
Median PFS (95% CI)	2.6 months (2.0–3.2)	–

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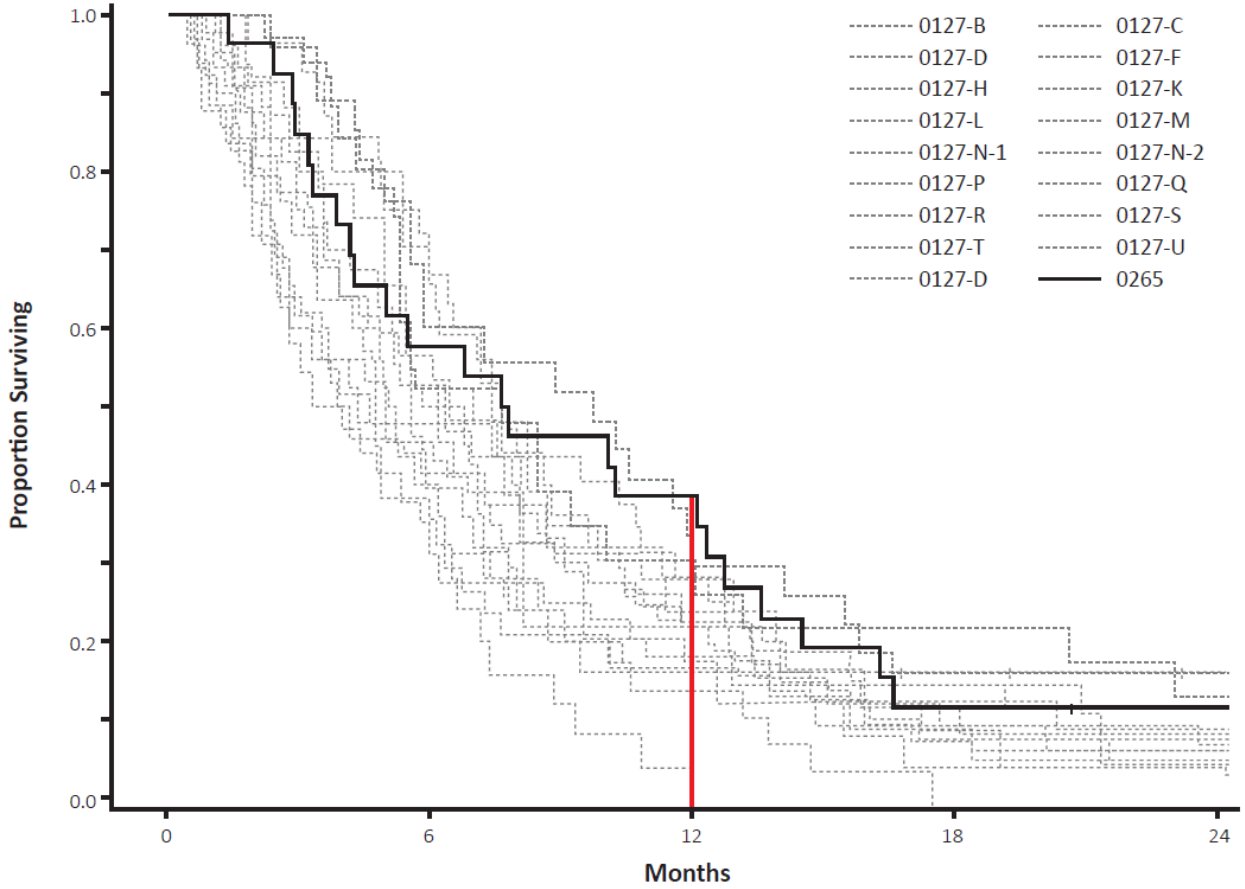
CI, confidence interval; NR, not reached.

GOG/NRG-0265: Survival in the Context of Historical GOG PRmCC Clinical Trials



1. Tewari KS, Monk BJ. *Curr Oncol Rep*. 2005;7(6):419-434; 2 Muggia F, et al. *Gynecol Oncol*. 2004;92(2):639-643; 3. Plaxe SC, et al. *Cancer Chemother Pharmacol.* 2002;50(2):151-154; 4. Armstrong DK, et al. *Invest New Drugs*. 2003;21(4):453-457; 5. Fracasso PM, et al. *Gynecol Oncol*. 2003;90(1):177-180; 6. Brewer CA, et al. *Gynecol Oncol*. 2006;100(2):385-388; 7. Rose P, et al. *Gynecol Oncol*. 2006;102(2):210-213; 8.Garcia AA, et al. *Am J Clin Oncol.* 2007;30(4):428-431; 9. Miller DS, et al. *Gynecol Oncol*. 2008;110(1):65-70; 10. Fiorica JV, et al. *Gynecol Oncol*. 2009;115(2):285-289; 11. Monk BJ, et al. *J Clin Oncol.* 2009;27(7):1069-1074; 12. Schilder RJ, et al. *Int J Gynecol Cancer.* 2009;19(5):929-933; 13. National Cancer Institute. Vaccine therapy in treating patients with persistent or recurrent cervical cancer. http://www.cancer.gov/about-cancer/treatment/clinical-trials/search/view?cdrid=691288. Accessed May 25, 2016;
14. Gynecologic Oncology Group/NRG Oncology. Data on file, 2016.

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Objective Response

OBJECTIVE RESPONSE

- Investigator assessment of tumor best response

	Stage 1 (N = 26)	Stage 2 (N = 24)
Tumor best response, n (%)		
CR	0 (0)	1 (4)
SD	7 (27)	8 (33)
PD	10 (38)	11 (46)
NE	6 (23)	4 (17)

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CR, complete response, NE, no evaluation; PD, progressive disease, SD, stable disease.

Safety/Tolerability – Stage 1

Adverse Event Summary (n=26)			
Adverse event (AE)	**Grade 1-4**	**Grade 3**	**Grade 4**
Patients with ≥ 1 treatment-related AE (TRAE), n (%)	24 (92)	4 (15)	1 (4)*
TRAEs occurring in ≥ 10% of patients			
Fatigue	15 (58)	-	-
Chills	14 (54)	-	-
Fever	11 (42)	-	-
Nausea	10 (39)	-	-
Headache	9 (35)	-	-
Hypotension	7 (27)	2 (8)	-
Vomiting	6 (23)	-	-
Cytokine release syndrome	5 (19)	3 (12)	-
Myalgia	5 (19)	-	-
Abdominal pain	4 (15)	-	-
General pain	4 (15)	-	-
Flu-like symptoms	3 (11)	-	-
AST elevation	3 (11)	-	-

Safety findings among patients enrolled in Stage 2 are similar to those reported in detail for Stage 1

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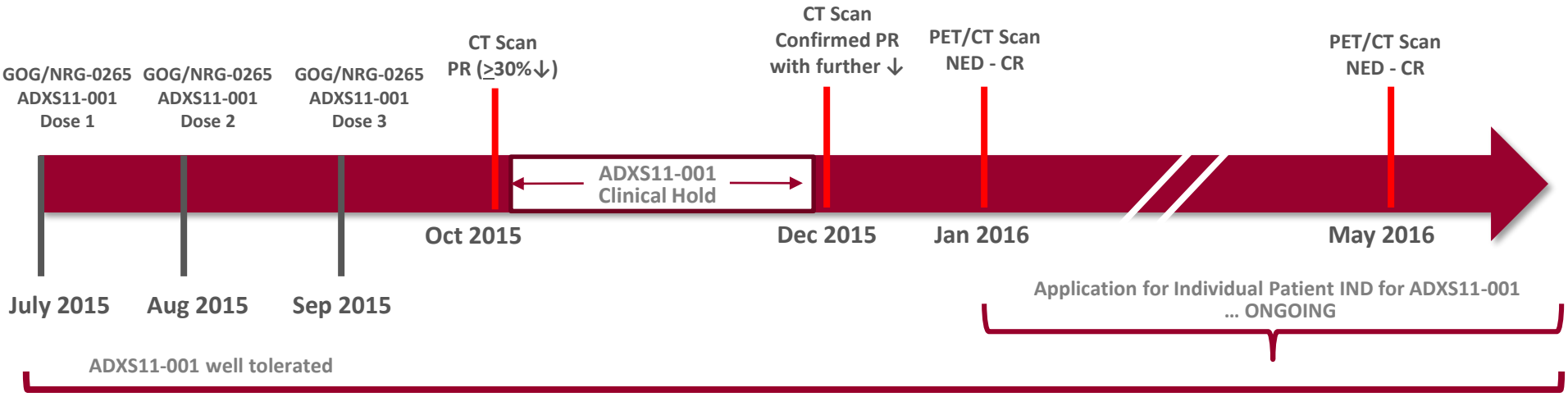
*The observed grade 4 TRAE recorded in one patient (lung infection and sepsis) was considered *possibly related* to treatment.
AE, adverse event;; AST, aspartate aminotransferase; TRAE, treatment-related AE.

GOG/NRG-0265 Case Study: Durable Complete Response to ADXS11-001

- 66-year-old woman diagnosed with squamous cell cancer of the cervix in 2006, surgically treated with radical hysterectomy in 2007
- Pelvic recurrence in 2014
  - Paclitaxel/carboplatin × 8 cycles (6 cycles with bevacizumab) → cisplatin (2 cycles) + pelvic radiation. Treatment completed August 2014
- Systemic recurrence June 2015
  - Enrolled in GOG/NRG-0265



Survival *to date* – second-line metastatic squamous cell cervical cancer (post-bevacizumab): 11 months

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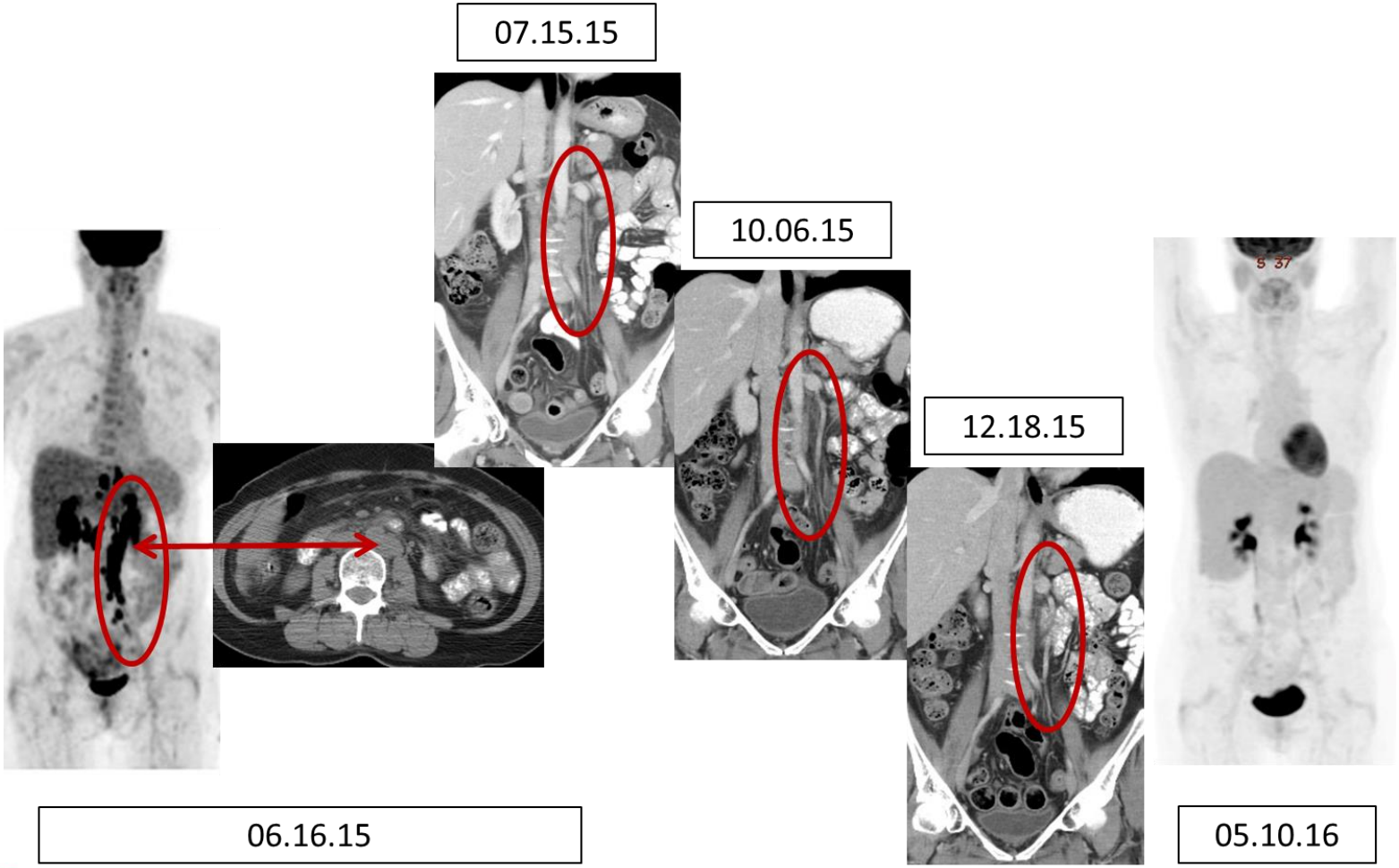
CT, computed tomography; IND, Investigational New Drug; NED, no evidence of disease; PET, positron emission tomography; PR, partial response.

GOG/NRG-0265 Case Study: Resolution of LN Mets (PET, Diagnostic CT)



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LN, lymph node; mets, metastases.

Conclusions

- In patients with PRmCC and progression following ≥1 prior lines of systemic therapy, ADXS11-001 is well tolerated and demonstrates a 38.5% rate of 12-month survival (n = 10/26)
- Although preliminary, findings from stage 2 reinforce the rationale for further controlled investigation of ADXS11-001 in PRmCC, and suggest consistent survival benefit in a heavily bevacizumab-pretreated population (31% vs 83% in stage 1 and stage 2, respectively), particularly among those patients receiving 3 or more doses of immunotherapy
- An international Advaxis-sponsored phase III study of ADXS11-001 as adjuvant treatment of high-risk locally advanced cervical cancer (AIM2CERV) is under development in collaboration with the GOG Foundation

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