Novartis AG
Investor Relations

Novartis Investor Call Highlights from ESMO

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Overview of Novartis at ESMO

47

abstracts have been accepted

7

oral presentations

13

Novartis brands/ compounds with data being presented

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Key messages

1. Alpelisib (BYL719) trial SOLAR-1 met primary endpoint in *PIK3CA*-mutant HR+/HER2- advanced breast cancer with manageable safety profile; submission in 4Q-2018

2. Tafinlar® + Mekinist® additional follow-up data in adjuvant melanoma demonstrate strong efficacy and durability after 44 months of follow-up

3. Lutathera® demonstrated significant improvement in progression-free survival (PFS) regardless of baseline liver tumor burden in patients with neuroendocrine tumor (NET)

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Agenda

1	**Alpelisib (BYL719) in HR+/HER2- advanced breast cancer with *PIK3CA* mutation**
2	Tafinlar® + Mekinist® in adjuvant melanoma
3	Lutathera® in advanced, progressive midgut neuroendocrine tumor (NET)

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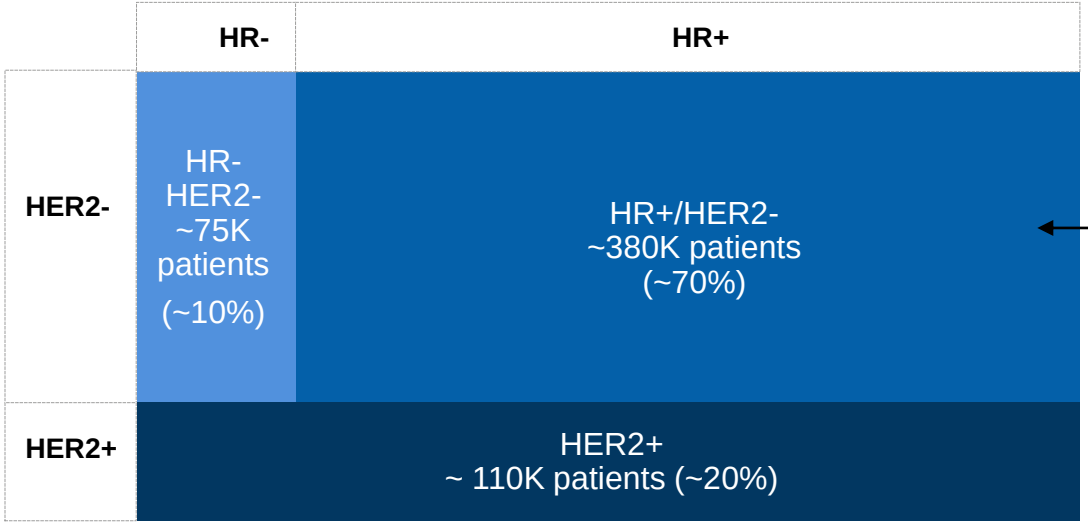
Alpelisib (BYL719), promising addition to portfolio, strengthening presence in HR+/HER2- breast cancer



Alpelisib (α-specific PI3K inhibitor):

- Prevalence of *PIK3CA* mutation is in approximately 40% of HR+/HER2- advanced breast cancer patients
- Alpelisib potentially represents an important therapy for patients with tumors harboring *PIK3CA* mutations

Source: Kantar 2017, G7 patients estimates.

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Novartis clinical trial programs advancing across indications for HR+/HER2- advanced breast cancer

	Trial	Indication	Opportunity	Status	Planned next milestone
Kisqali®	**MONALEESA-2**	1st line in combination with letrozole	CDK 4/6 in combination with SoC	Launched globally	
	MONALEESA-3	1st & 2nd line in combination with fulvestrant	1st CDK 4/6 with Phase 3 study with fulvestrant	Approved in US Submitted in EU RoW submissions ongoing	EU (2Q-2019) & RoW approvals & launch
	MONALEESA-7	Pre-menopausal women 1st line in combination with goserelin + ET	1st CDK 4/6 in Pre-menopausal setting	Approved in US Submitted in EU RoW submissions ongoing	EU (2Q-2019) & RoW approvals & launch
	NATALEE	Adjuvant HR+ breast cancer patients	CDK 4/6 in combination with SoC	Trial initiation	FPFV planned for 1Q-2019
Alpelisib (BYL719)	**SOLAR-1**	*PIK3CA*-mutant advanced breast cancer in combination with fulvestrant following progression on an ET based regimen	1st & only α-specific PI3Ki for *PIK3CA* mutated HR+/HER2- advanced breast cancer. In combination with fulvestrant	Met primary endpoint Ongoing discussions with HAs	Data release at ESMO; regulatory submissions to start in 4Q-2018

ET, Endocrine Therapy. FPFV, first patient first visit. HAs, Health Authorities. RoW, rest of world. SoC, Standard of Care.

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Unmet need in patients with HR+/HER2– advanced breast cancer

- First-line treatment for HR+/HER2– advanced breast cancer is endocrine therapy, with/without a CDK 4/6 inhibitor[1-3]. Acquired resistance to endocrine therapy remains a challenge for these patients[4-6]
- Activation of the PI3K pathway can occur due to *PIK3CA* mutations, present in ~40% of patients with HR+/HER2– breast cancer[7-9], and has been implicated in resistance to endocrine therapies[10,11]
- *PIK3CA* gene mutations occur in various solid tumors including colon, glioblastoma, gastric, breast, ovarian, endometrial, lung, head/neck squamous cell cancers[12], and prostate cancer[13]

1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer. V2.2018. 2. Cardoso F, et al. Ann Oncol 2018;29:1634–57. 3. Rugo H, et al. J Clin Oncol 2016;34:3069–103. 4. Shah PD & Dickler MN. Clin Adv Hematol Oncol 2014;12:214–23. 5. Liu C, et al. J Steroid Biochem Mol Biol 2017;172:166–75. 6. Ciruelos Gil EM. Cancer Treat Rev 2014;40:862–71. 7. Cancer Genome Atlas Network. Nature 2012;490:61–70. 8. Mollon L, et al. AACR 2018 (poster 2107). 9. Arthur LM, et al. Breast Cancer Res Treat 2014;147:211–9. 10. Miller TW, et al. J Clin Oncol 2011;29:4452–61. 11. Bosch A, et al. Sci Transl Med 2015;7:283. 12. Ligresti G et al. Cell Cycle 2009;8:9, 1352-1358 . 13. Pearson H, et al. Cancer Discovery 2018;8(6):764-779.

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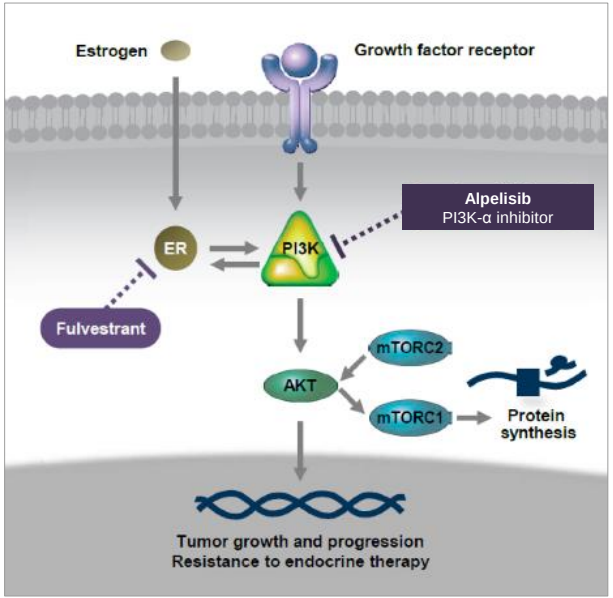
Alpelisib: Potent, specific inhibitor of PI3K-α



Alpelisib (BYL719) is a highly selective, oral inhibitor of the PI3K α-isoform[1,2]

Alpelisib specifically inhibits the PI3K-α isoform, thus avoiding the cumulative toxicity associated with inhibition of all four PI3K isoforms[3]

Alpelisib has demonstrated antitumor activity in a number of cancer cell lines and tumor xenograft models, especially those harboring *PIK3CA* alterations[4,5]

ER, estrogen receptor; PI3K, phosphatidylinositide 3-kinase; mTOR, mechanistic target of rapamycin; AKT, protein kinase B

1. Fritsch C et al. *Mol Cancer Ther* 2014;13:1117–1129. 2. Osborne CK, Schiff R. *Annu Rev Med* 2011; 62:233–247. 3. Greenwell, IB, et al. Oncology 2017;31(11):821-828. 4. Miller TW, *et al. J Clin Oncol* 2011;29:4452–61. 5. Bosch A, *et al. Sci Transl Med* 2015;7:283.

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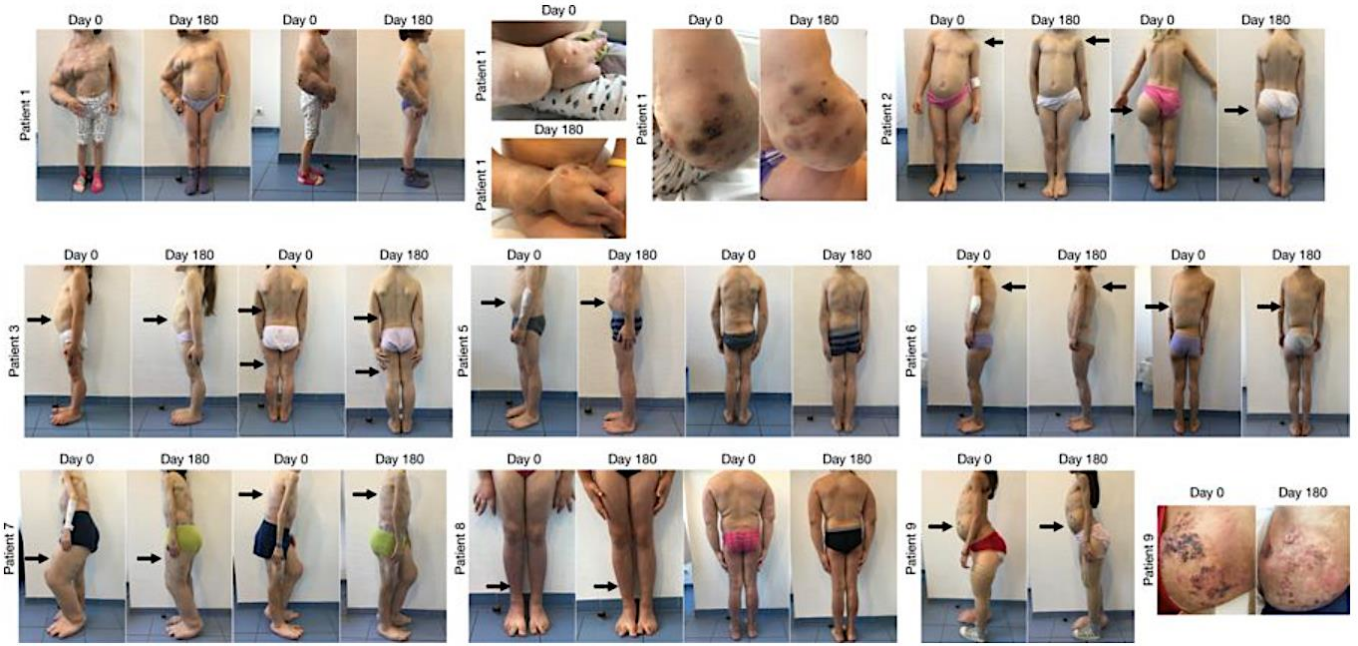
Efficacy of alpelisib in patients with PROS after 6 months of treatment



PROS. *PIK3CA*-related overgrowth spectrum.
Source: Venot Q., et al. *Nature* 2018;*558*(7711):540.

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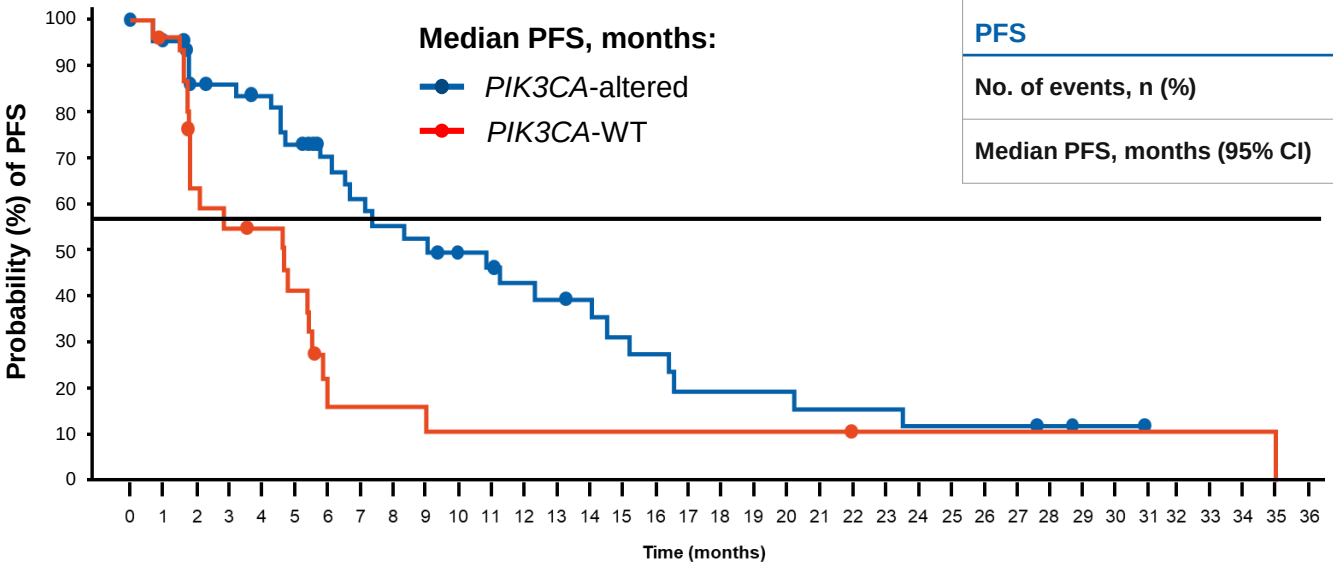
Previous PhIb trial of alpelisib + fulvestrant showed promising antitumor activity in *PIK3CA*-mutant tumors



PFS	*PIK3CA*-altered (n=49)	*PIK3CA*-WT (n=32)
No. of events, n (%)	29	21
Median PFS, months (95% CI)	9.1 (6.6-14.6)	4.7 (1.9-5.6)

Juric D, *et al. JAMA Oncology,* 2018 (accepted). Data from an earlier data cutoff was presented at Miami Breast Cancer Conference 2016.

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SOLAR-1: PhIII randomized, controlled trial (NCT02437318)

Key eligibility criteria

Men or postmenopausal women, with HR+/HER2- ABC

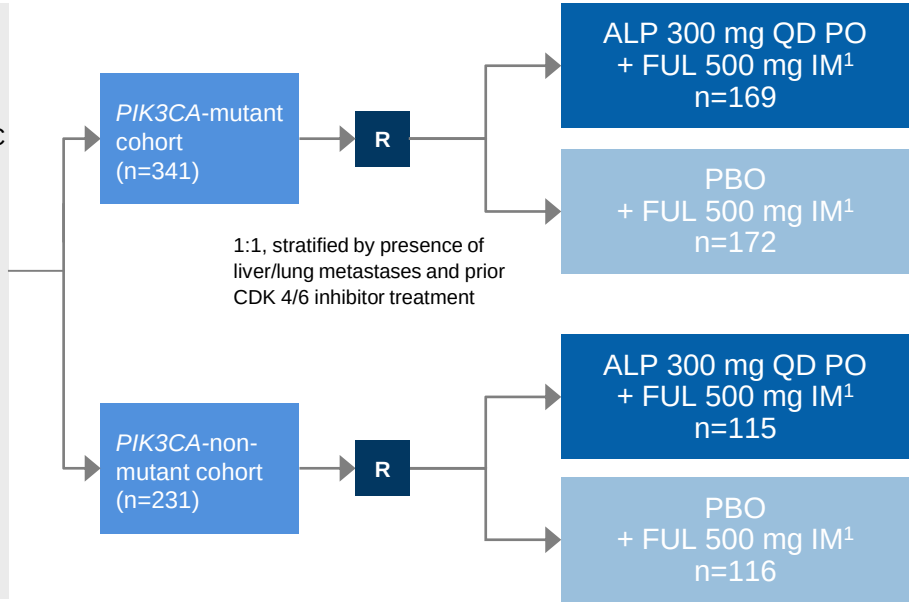
Recurrence/progression on/after prior AI

Identified *PIK3CA* status (in archival or fresh tumor tissue)

Measurable disease or ≥1 predominantly lytic bone lesion

ECOG performance status ≤1

(n=572)



Primary endpoint

PFS (locally assessed) in *PIK3CA*-mutant cohort

Secondary endpoints include:

OS (*PIK3CA*-mutant cohort)

PFS (*PIK3CA*-non-mutant cohort)

PFS (*PIK3CA*-mutation in ctDNA)

OS (*PIK3CA*-non-mutant cohort)

ORR

Safety

*Fulvestrant given on Day 1 and Day 15 of the first 28-day cycle, then Day 1 of subsequent 28-day cycles. ABC, advanced breast cancer; AI, aromatase inhibitor; ALP, alpelisib; CBR, clinical benefit rate; CT, chemotherapy; ctDNA, circulating tumor DNA ECOG, Eastern Cooperative Oncology Group; ET, endocrine therapy; FUL, fulvestrant; IM, intramuscular; ORR, overall response rate; OS, overall survival; PBO, placebo; PFS, progression-free survival; PO, orally; QD, daily; R, randomization.

Source: Andre F, Ciruelos EM, Rubovszky G et al. Alpelisib + fulvestrant for HR+, HER2- advanced breast cancer: Results of the Phase III SOLAR-1 trial. Presented at the European Society for Medical Oncology (ESMO) 2018 Congress (Abstract LBA3_PR) on October 20, 2018.

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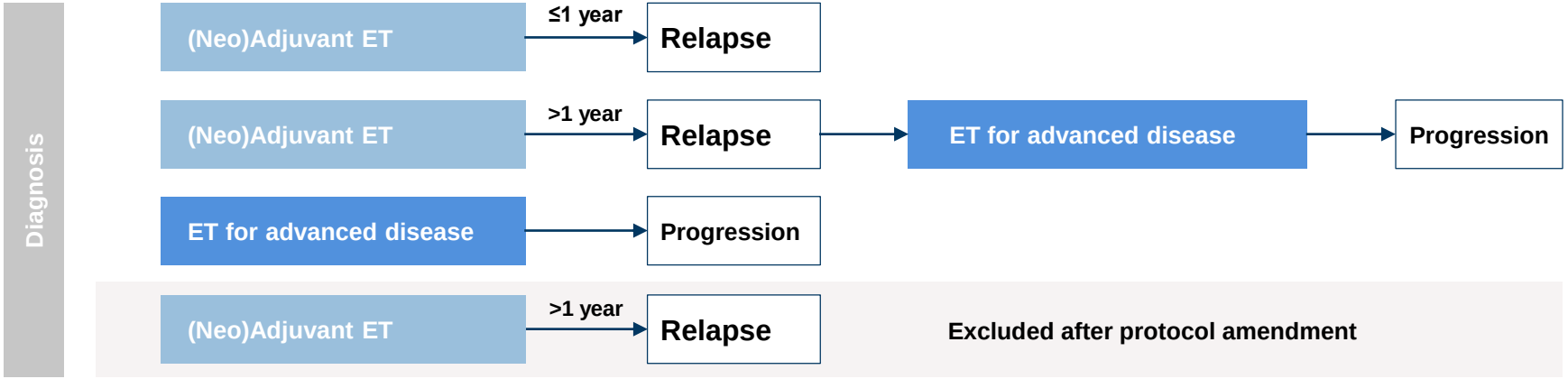
Inclusion criteria: Prior exposure to aromatase inhibitor



Patients who had received one prior line of endocrine therapy were enrolled

- Endocrine resistance and endocrine sensitivity were defined according to the ESMO guidelines[1]
- Patients who had not received endocrine therapy for advanced breast cancer were considered “first line”

1. Cardoso F, et al. *Ann Oncol* 2018;29:1634–57.

Source: Andre F, Ciruelos EM, Rubovszky G et al. Alpelisib + fulvestrant for HR+, HER2- advanced breast cancer: Results of the Phase III SOLAR-1 trial. Presented at the European Society for Medical Oncology (ESMO) 2018 Congress (Abstract LBA3_PR) on October 20, 2018.

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Patient disposition

Disposition[1]	*PIK3CA*-mutant		*PIK3CA*-non-mutant	
	Alpelisib + fulvestrant (N=169)	**Placebo + fulvestrant** (N=172)[2]	**Alpelisib + fulvestrant** (N=115)	**Placebo + fulvestrant** (N=116)
On treatment	42 (24.9)	32 (18.6)	13 (11.3)	14 (12.1)
Discontinued	127 (75.1)	139 (80.8)	102 (88.7)	102 (87.9)
Reasons for discontinuation				
Adverse event[3]	5 (3.0)	3 (1.7)	9 (7.8)	0
Death	3 (1.8)	4 (2.3)	1 (0.9)	0
Physician decision	6 (3.6)	6 (3.5)	5 (4.3)	4 (3.4)
Progressive disease	93 (55.0)	117 (68.0)	80 (69.6)	91 (78.4)
Protocol deviation	4 (2.4)	3 (1.7)	1 (0.9)	3 (3.4)
Subject/Guardian decision	16 (9.5)	6 (3.5)	6 (5.2)	4 (3.4)
Median follow-up (months)	20.2	19.9	7.3	7.4

1. Characteristics are n (%) unless otherwise stated. 2. 1 patient in the *PIK3CA*-mutant cohort randomized to placebo was not treated due to protocol deviation 3. Includes those patients who discontinued both, Alpelisib / placebo and fulvestrant.

Source: Andre F, Ciruelos EM, Rubovszky G et al. Alpelisib + fulvestrant for HR+, HER2- advanced breast cancer: Results of the Phase III SOLAR-1 trial. Presented at the European Society for Medical Oncology (ESMO) 2018 Congress (Abstract LBA3_PR) on October 20, 2018.

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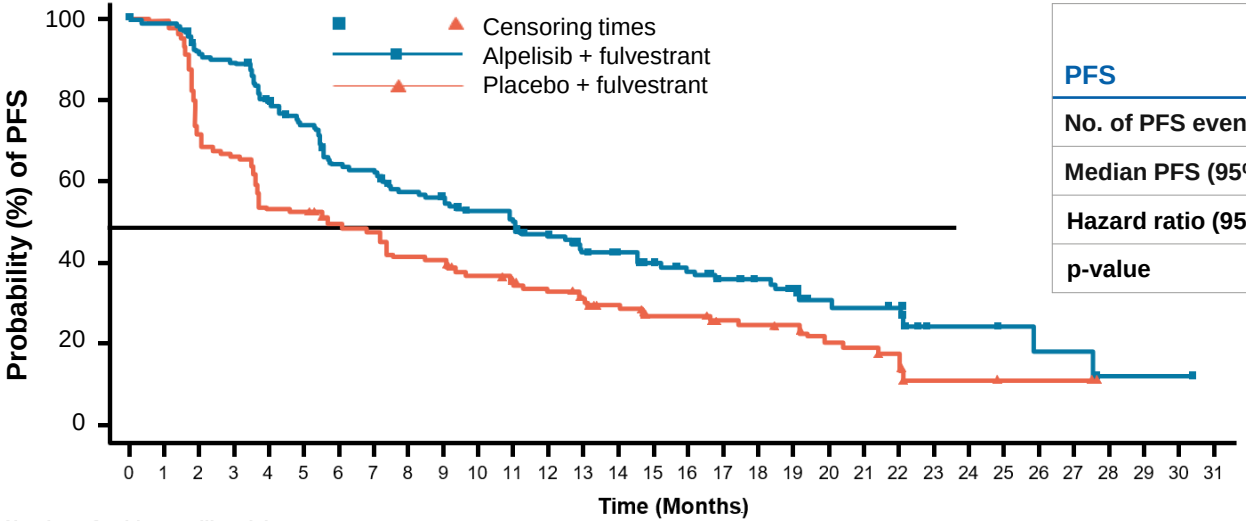
New data at ESMO: Study met primary endpoint of PFS in the *PIK3CA*-mutant cohort



PFS	Alpelisib + fulvestrant (N=169)	Placebo + fulvestrant (N=172)
No. of PFS events, n (%)	103 (60.9)	129 (75.0)
Median PFS (95% CI)	11.0 (7.5-14.5)	5.7 (3.7-7.4)
Hazard ratio (95% CI)	0.65 (0.50-0.85)	
p-value	0.00065	

Number of subjects still at risk

Alpelisib + Fulv	169	158	145	141	123	113	97	95	85	82	75	71	62	54	50	43	39	32	30	27	17	16	14	5	5	4	3	3	1	1	1	0
Placebo + Fulv	172	167	120	111	89	88	80	77	67	66	58	54	48	41	37	29	29	21	20	19	14	13	9	3	3	2	2	2	0	0	0	0

Overall survival data immature at this time and will discussed at a later date.

Source: Andre F, Ciruelos EM, Rubovszky G et al. Alpelisib + fulvestrant for HR+, HER2- advanced breast cancer: Results of the Phase III SOLAR-1 trial. Presented at the European Society for Medical Oncology (ESMO) 2018 Congress (Abstract LBA3_PR) on October 20, 2018.

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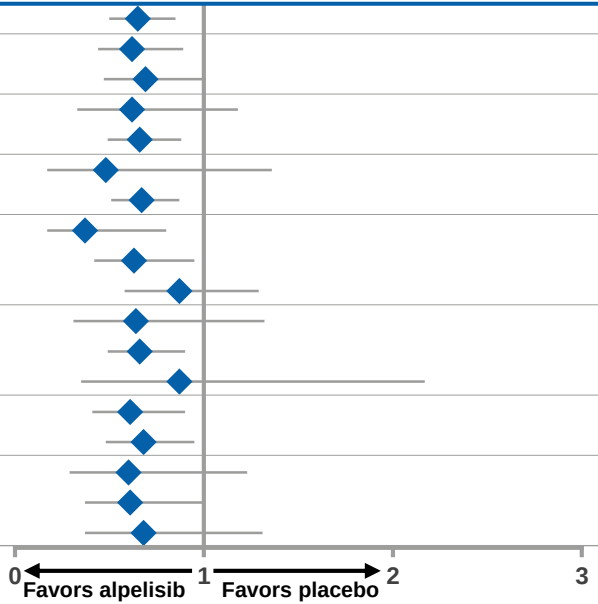
Similar benefit of alpelisib across multiple key subgroups in *PIK3CA*-mutant cohort

Subgroup		No. of patients	Hazard Ratio (95% CI)
All subjects		341	0.65 (0.50–0.85)
Lung/liver metastases	Yes	170	0.62 (0.44–0.89)
	No	171	0.69 (0.47–1.01)
Bone-only disease	Yes	77	0.62 (0.33–1.18)
	No	264	0.66 (0.49–0.88)
Prior CDK 4/6 inhibitor treatment	Yes	20	0.48 (0.17–1.36)
	No	321	0.67 (0.51–0.87)
Prior chemotherapy	Neoadjuvant	46	0.37 (0.17–0.80)
	Adjuvant	161	0.63 (0.42–0.95)
	None	133	0.87 (0.58–1.29)
Endocrine status	Primary resistance	45	0.64 (0.31–1.32)
	Secondary resistance	247	0.66 (0.49–0.90)
	Sensitive	39	0.87 (0.35–2.17)
PIK3CA mutation exon	Exon 9	165	0.61 (0.41–0.90)
	Exon 20	193	0.68 (0.48–0.95)
PIK3CA mutation subtype[1]	*E542K*	60	0.60 (0.29–1.23)
	E545X†	105	0.61 (0.37–1.00)
	H1047X†	193	0.68 (0.48–0.95)



1. Mutations detected in tissue. Patients may have had more than one *PIK3CA* mutation; †Includes multiple subtypes of *E545* and *H1047*.

Source: Andre F, Ciruelos EM, Rubovszky G et al. Alpelisib + fulvestrant for HR+, HER2- advanced breast cancer: Results of the Phase III SOLAR-1 trial. Presented at the European Society for Medical Oncology (ESMO) 2018 Congress (Abstract LBA3_PR) on October 20, 2018.

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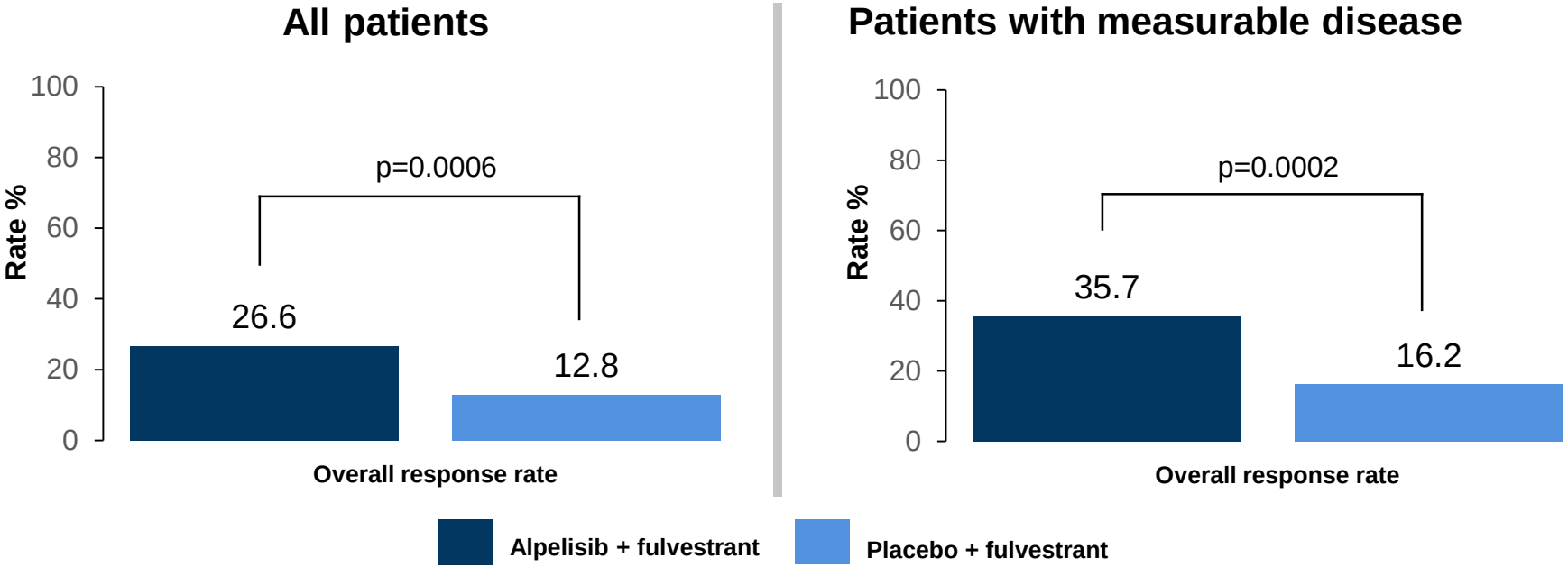
Overall response rate in the *PIK3CA*-mutant cohort



ORR = complete response + partial response.

Source: Andre F, Ciruelos EM, Rubovszky G et al. Alpelisib + fulvestrant for HR+, HER2- advanced breast cancer: Results of the Phase III SOLAR-1 trial. Presented at the European Society for Medical Oncology (ESMO) 2018 Congress (Abstract LBA3_PR) on October 20, 2018.

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Adverse events; safety profile manageable

AEs ≥20% in either arm, %	Alpelisib + fulvestrant N=284			Placebo + fulvestrant N=287		
	All	Grade 3	Grade 4	All	Grade 3	Grade 4
Any adverse event	282 (99.3)	183 (64.4)	33 (11.6)	264 (92.0)	87 (30.3)	15 (5.2)
Hyperglycemia	181 (63.7)	93 (32.7)	11 (3.9)	28 (9.8)	1 (0.3)	1 (0.3)
Diarrhea	164 (57.7)	19 (6.7)	0	45 (15.7)	1 (0.3)	0
Nausea	127 (44.7)	7 (2.5)	0	64 (22.3)	1 (0.3)	0
Decreased appetite	101 (35.6)	2 (0.7)	0	30 (10.5)	1 (0.3)	0
Rash	101 (35.6)	28 (9.9)	0	17 (5.9)	1 (0.3)	0
Vomiting	77 (27.1)	2 (0.7)	0	28 (9.8)	1 (0.3)	0
Decreased weight	76 (26.8)	11 (3.9)	0	6 (2.1)	0	0
Stomatitis	70 (24.6)	7 (2.5)	0	18 (6.3)	0	0
Fatigue	69 (24.3)	10 (3.5)	0	49 (17.1)	3 (1.0)	0
Asthenia	58 (20.4)	5 (1.8)	0	37 (12.9)	0	0

Hyperglycemia was the most frequent AE leading to treatment discontinuation (18 patients [6.3%] in the alpelisib arm and no patients in the placebo arm)

19 on-treatment deaths were observed; 7 (2.5%) and 12 (4.2%) in the alpelisib and placebo arms, respectively. 2 in alpelisib arm and 4 in placebo arm died due to causes other than study indication (all were unrelated to study treatment)

Source: Andre F, Ciruelos EM, Rubovszky G et al. Alpelisib + fulvestrant for HR+, HER2- advanced breast cancer: Results of the Phase III SOLAR-1 trial. Presented at the European Society for Medical Oncology (ESMO) 2018 Congress (Abstract LBA3_PR) on October 20, 2018.

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Key takeaways

1. **~40% of HR+/HER2– breast cancer patients have a *PIK3CA* mutation,** which is associated with poor prognosis; currently there are no treatments that target this mutation
2. Alpelisib plus fulvestrant **significantly improved PFS and ORR in patients with *PIK3CA* mutated HR+/HER2- advanced breast cancer**[1]
3. Alpelisib is the **first and only investigational alpha-specific PI3K inhibitor to show superior PFS and predictable, manageable tolerability**
4. Health authority interactions have been initiated and regulatory submissions are planned to start in 4Q-2018

[1] Following progression on or after an aromatase inhibitor with or without a CDK 4/6 inhibitor, vs. fulvestrant alone.

Agenda

1	Alpelisib (BYL719) in HR+/HER2- advanced breast cancer with *PIK3CA* mutation
2	**Tafinlar® + Mekinist® in adjuvant melanoma**
3	Lutathera® in advanced, progressive midgut NET

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COMBI-AD study design – extended follow-up analysis out to 44 months

Tafinlar (dabrafenib) + Mekinist (trametinib)

Key eligibility criteria

Completely resected stage IIIA (lymph node metastasis > 1 mm), IIIB, or IIIC cutaneous melanoma

BRAF V600E/K mutation

ECOG performance status 0 or 1

No prior radiotherapy or systemic therapy

Tissue collection was mandatory at baseline and optional upon recurrence

Stratification

- *BRAF* mutation status (V600E, V600K)
- Disease stage (IIIA, IIIB, IIIC)

RANDOMIZATION

1:1

N = 870

Dabrafenib 150 mg BID + Trametinib 2 mg QD (n = 438)

2 matched placebos (n = 432)

Treatment duration: 12 months[a]

Primary analysis[b] D + T median FU, 33 months

Updated analysis D + T median FU, 44 months

Primary endpoint: Relapse-Free Survival

Secondary endpoints: OS[c], DMFS, FFR, safety

BID, twice daily; DMFS, distant metastasis–free survival; ECOG, Eastern Cooperative Oncology Group; FFR, freedom from relapse; FU, follow-up; QD, once daily;
a. Or until disease recurrence, death, unacceptable toxicity, or withdrawal of consent; b. Study was designed to provide > 90% power (assuming ≈ 410 RFS events observed) to detect an HR of 0.71 with an overall 2-sided type I error rate of 5%. New primary melanoma considered as an event. c. OS was to be tested only if the primary endpoint (RFS) significantly favoured the combination arm. Long GV, et al. N Engl J Med. 2017;377:1813-1823.

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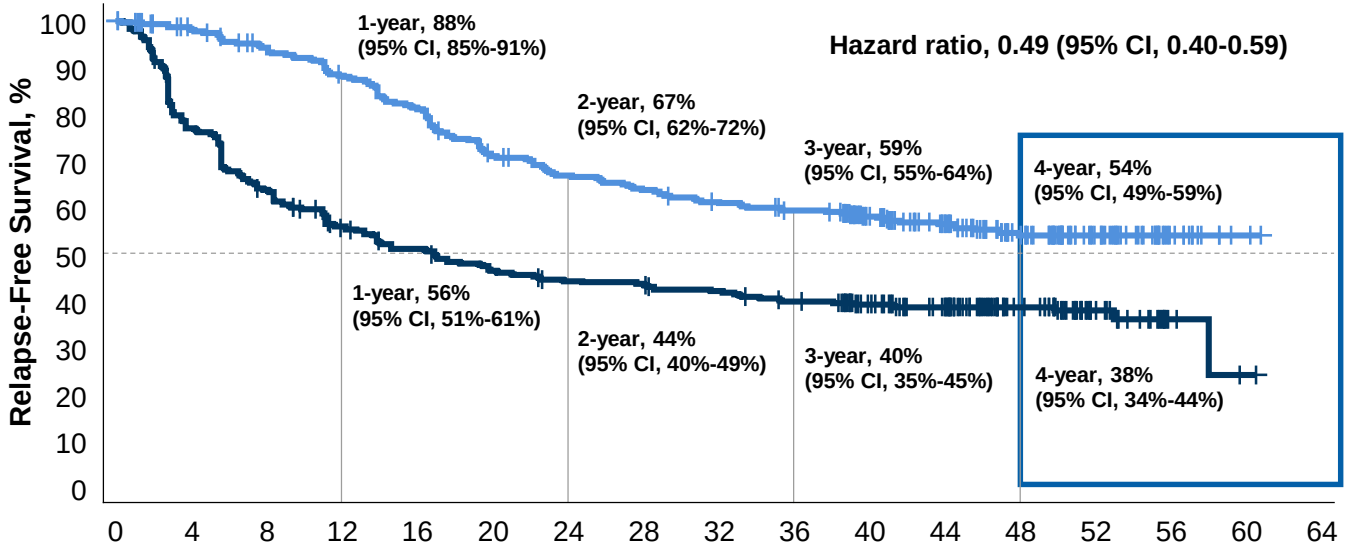
Relapse-Free Survival: Kaplan-Meier curves remain separated after additional follow-up



No. at Risk																
Dabrafenib plus trametinib	438	405	381	354	324	281	262	249	236	227	183	148	92	47	13	2	0
Placebo	432	322	263	219	198	178	168	164	157	147	128	107	63	27	4	1	0

Source: G. Long, et al. COMBI-AD RFS Update and Biomarker Analysis. Abstract LBA43. 2018 European Society of Medical Oncology (ESMO), October 19-23, 2018, Munich, Germany.

Key takeaways

Tafinlar® (dabrafenib) + Mekinist® (trametinib)

1. COMBI-AD extended follow-up analysis out to 44 months[1] confirm leading BRAF/MEK inhibitor combination Tafinlar® + Mekinist® continues to show relapse free survival benefit. 4-year RFS rates were 54% with adjuvant Tafinlar® + Mekinist® vs 38% with placebo

2. Tafinlar® + Mekinist® approved for adjuvant melanoma in all major markets in 2018

3. Cure rate modeling[2] estimating fraction of patients who may not relapse was 54% with adjuvant Tafinlar® + Mekinist® compared to 37% with placebo

1. Tafinlar® + Mekinist® arm median follow up was 44 months. Placebo arm median was 42 months
2. The fraction of patients remaining relapse free long term was estimated using a Weibull mixture cure-rate model

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Agenda

1	Alpelisib (BYL719) in HR+/HER2- advanced breast cancer with *PIK3CA* mutation
2	Tafinlar® + Mekinist® in adjuvant melanoma
3	**Lutathera® in advanced, progressive midgut NET**

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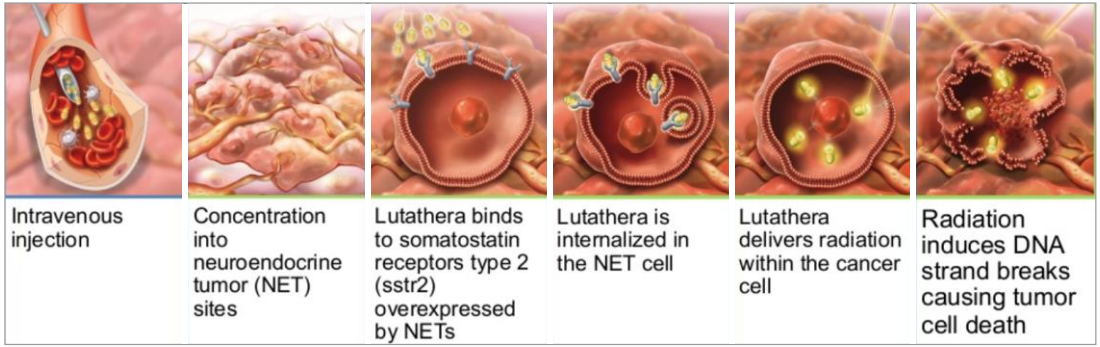
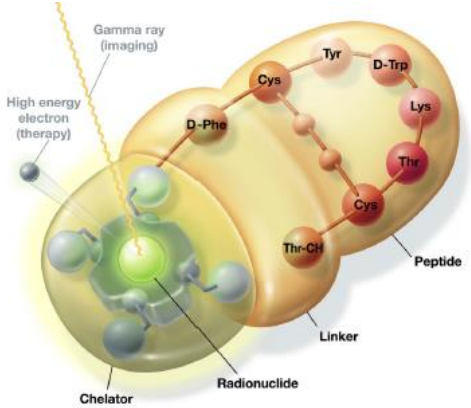
Overview of Lutetium Lu 177 Dotatate[1] (Lutathera®[2])

- Lutathera® belongs to an innovative drug category called **RadioLigand Therapy (RLT).** RLT involves the systemic administration of a radiopharmaceutical to deliver cytotoxic radiation to a tumor
- Lutetium Lu 177 dotatate is composed of a lutetium 177 radionuclide chelated to a peptide. Lutetium emits mostly high energy electrons (β-particles; half-life 6.6 days)
- The peptide is designed to target somatostatin receptors with high binding affinity





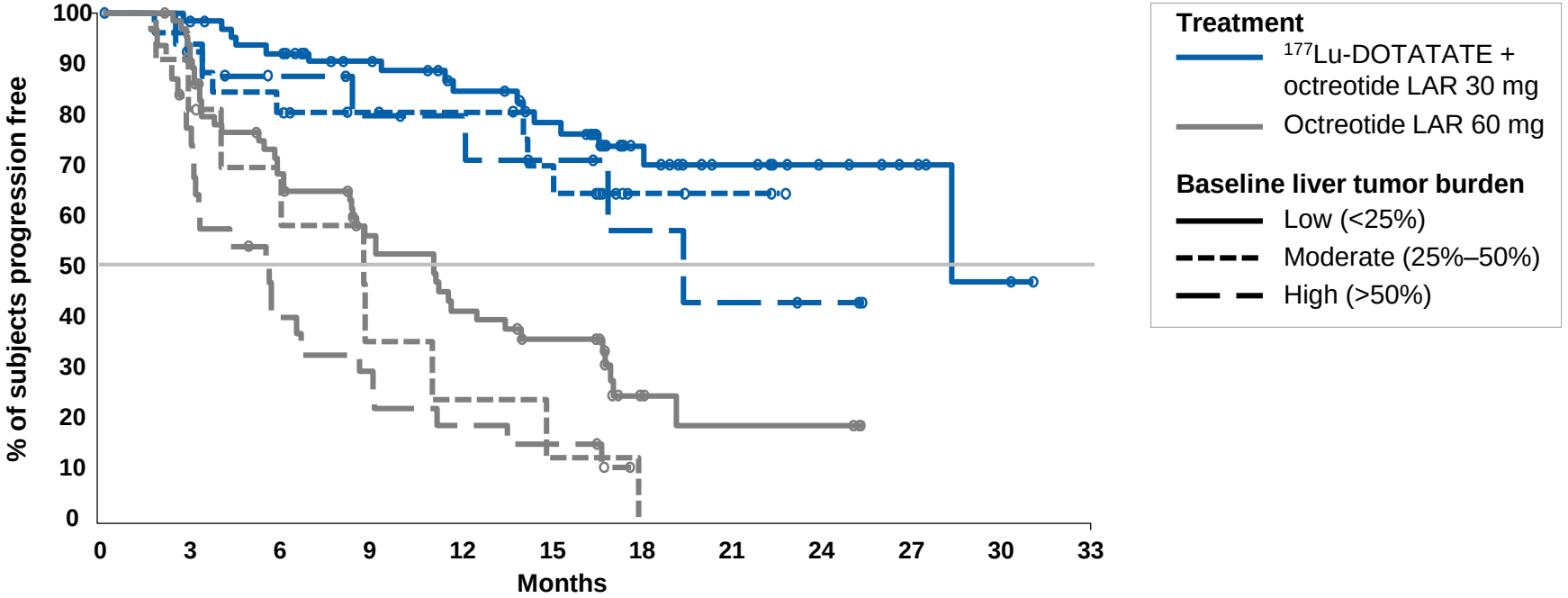
1. USAN: lutetium Lu 177 dotatate / INN: lutetium (177Lu) oxodotreotide
2. Lutathera® is a registered trademark of Advanced Accelerator Applications

High liver tumor burden associated with worse prognosis in metastatic NETs

- 6.98/100,000 patients are diagnosed every year with NETs,[1] and due to frequent delays in accurate diagnosis, many patients already have advanced disease; Less than 50% of patients with metastatic NETs survive 5-years[2,3]
- Metastases are predominantly (88%) found in the liver of patients with small intestine NET[4]; Patients with metastatic midgut NET and a high liver tumor load at diagnosis have a poorer prognosis than patients with few liver metastases[5,6]
- Lutathera® was approved in the EU in 2017 and in the US in 2018 with plans to expand registration in other geographies

1. Dasari A, et al. JAMA Oncol. 2017; 3(10):1335-1342. 2.Yao JC et al . J Clin Oncol 2008;26:3063-3072. 3. Modlin IM et al. Cancer 2003;97:934-959. 4. Riihimäki M, et al. *Int J Cancer.* 2016;139(12):2679-2686. 5. Rinke A, et al. *J Clin Oncol.* 2009;27(28):4656-4663. 6. Rinke A, et al. *Neuroendocrinology.* 2017;104(1):26-32.

Lutathera® demonstrated clinically relevant prolongation in median PFS compared with octreotide regardless of the extent of baseline liver tumor burden



Strosberg J, Hendifar A, Yao JC, et al. (2018, October) Impact of Liver Tumor Burden on Therapeutic Effect of 177Lu-DOTATATE Treatment: Analysis of Progression-Free Survival, Safety and Quality of Life in NETTER-1. Poster presented at the Annual Congress of the European Society for Medical Oncology, Munich, Germany.

Key takeaways

1. Lutathera® demonstrated significant prolongation in median PFS compared with octreotide LAR 60 mg in patients with advanced, progressive midgut NET regardless of baseline liver tumor burden
2. Patients with large (>30mm diameter) liver lesion or with elevated baseline alkaline phosphatase (ALP) liver enzyme also benefit from Lutathera®
3. Lutathera® treatment was associated with a clinically significant reduction in the estimated risk for deterioration of global health status (self-assessment of overall health and quality of life) vs comparator, regardless of baseline liver tumor burden
4. Further investigations of Lutathera® in other indications and combinations are planned

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Conclusions

1. Alpelisib met primary endpoint in *PIK3CA* mutations with manageable safety profile; on track to begin submissions in 4Q-2018

2. Tafinlar® + Mekinist® additional follow-up data demonstrate strong efficacy and durability after 40+ months (one of few treatments with this length of data)

3. AAA Lutathera® demonstrated significant improvement in PFS regardless of baseline liver tumor burden

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Other key highlights across disease areas

Breast cancer	Kisqali® (Ribociclib)	**MONALEESA-3**: In addition to significantly prolonging PFS in postmenopausal women with HR+/HER2- ABC, treatment with RIB + FUL (vs PBO + FUL) resulted in early tumor size reduction, a higher response rate and maintained or improved quality of life	**Oral**
		MONALEESA-7: In premenopausal women with HR+/HER2- ABC, treatment with RIB + FUL (vs PBO + FUL) maintained or improved HRQoL without negatively impacting physical activity and work productivity and led to clinically meaningful reductions in pain	**Oral**
Lung cancer	Capmatinib (INC280)	Results from the phase II **GEOMETRY-*mono*-1** study demonstrate clinically meaningful response rate and position capmatinib as potential best in class MET inhibitor for patients with *METΔex14* advanced NSCLC	**Oral**
Melanoma	Tafinlar® + Mekinist® (Dabrafenib + Trametinib)	**KEYNOTE-022**: Merck led trial of Pembro+D+T vs PBO+D+T demonstrated numerically longer PFS and DOR and a higher rate of G3-5 TRAEs in advanced melanoma	**Oral**

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SOLAR-1 demographics and baseline characteristics comparable between the two arms

	PIK3CA-mutant (DCO: 12-Jun-2018)		*PIK3CA*-non-mutant (DCO: 12-Jun-2018)	
	Alpelisib 300mg gd+ fulvestrant (N=169) n(%)	**Placebo qd+ fulvestrant** (N=172) n(%)	**Alpelisib 300mg gd+ fulvestrant** (N=115) n(%)	**Placebo qd+ fulvestrant** (N=116) n(%)
Median age, years (range)	63 (25-87)	64 (38-92)	62 (39-82)	63 (32-88)
<65	95 (56.2)	89 (51.7)	72 (62.6)	65 (56.0)
≥65	74 (43.8)	83 (48.3)	43 (37.4)	51 (44.0)
Race – n (%)				
White	117 (69.2)	109 (63.4)	82 (71.3)	69 (59.5)
Asian	34 (20.1)	40 (23.2)	25 (21.7)	26 (22.4)
Other[1]	18 (10,6)	23 (13,6)	8 (4,7)	21 (12,4)
Measurable disease	126 (74.6)	136 (79.1)	91 (79.1)	94 (81.0)
Visceral disease	93 (55.0)	100 (58.1)	66 (57.4)	74 (63.8)
Bone only disease	42 (24.9)	35 (20.3)	26 (22.6)	23 (19.8)
<3 met. sites of disease	121 (71.6)	113 (65.7)	79 (68.7)	71 (61.2)
Lung or liver mets[2]	84 (49.7)	86 (50.0)	56 (48.7)	56 (48.3)
Prior CDK 4/6i use[2]	9 (5.3)	11 (6.4)	7 (6.1)	8 (6.9)

Source: briefing book Table 3-8. 1. Other includes American Indian/Alaska, Black/African American, Other, and Unknown. 2. Randomization stratification factor.

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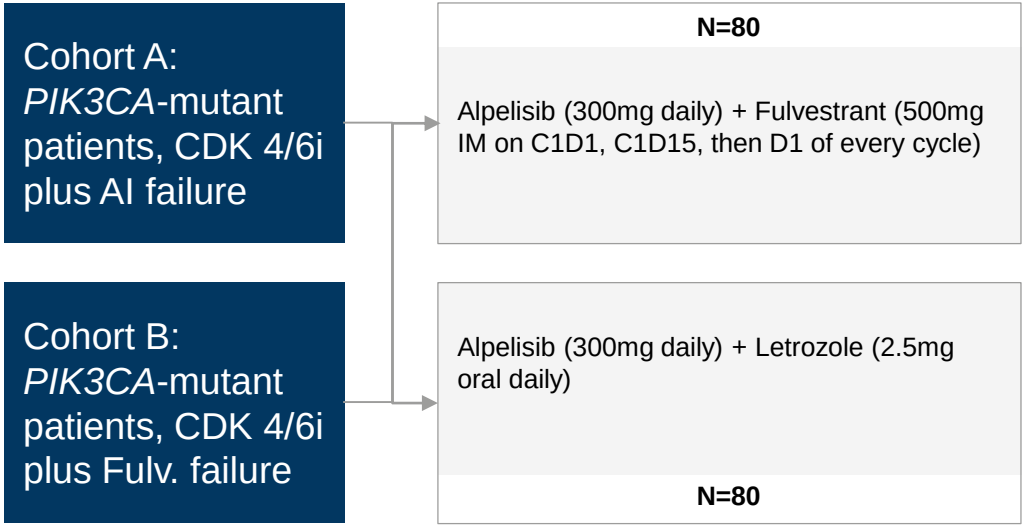
BYLieve study will address questions related to post CDK 4/6 sequencing



Primary endpoint
Proportion of patients alive without PD at 6 months in Cohort A and Cohort B

Secondary endpoints
- ✓ PFS
- ✓ PFS2
- ✓ ORR
- ✓ CBR
- ✓ Duration of Response
- ✓ Safety and tolerability

Exploratory biomarkers
Frequency of *PIK3CA* mutations in ctDNA and correlation with response

Global Phase II study in *PIK3CA-mutant* HR+/HER2- advanced breast cancer patients investigating alpelisib in combination with fulvestrant or AI, depending on prior ET therapy, in patients who have progressed on after receiving a CDK 4/6i +ET

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Impact of liver tumor burden on treatment outcomes with Lutathera® in the NETTER-1 study

Aim

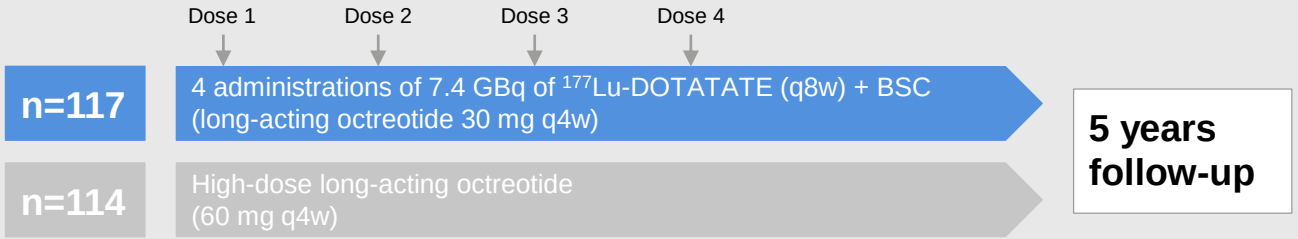
Evaluate the efficacy and safety of ^{177}Lu-DOTATATE + BSC compared with high-dose long-acting octreotide in patients with inoperable, locally advanced or metastatic, somatostatin receptor positive, midgut NET with radiologic PD under a standard dose of long-acting octreotide (20-30 mg q3-4w)

Design

International, multicenter, randomized, comparator-controlled, parallel-group, phase 3 trial

Treatment and assessments
Progression-free survival (central RECIST) every 12 weeks
Safety (NCI CTAE v4.03) every 2-12 weeks

Randomization
Stratified by
Highest tumor uptake by SRS (Krenning scale: grade 2, 3 or 4)
Duration of constant-dose long-acting octreotide (≤6 or >6 months)



BSC, best supportive care: CTCAE, Common Terminology Criteria for Adverse Events; NCI, National Cancer Institute; PD, progressive disease; q3-4w, every 3-4 weeks; q4w, every 4 weeks; q8w, every 8 weeks; RECIST, Response Evaluation Criteria in Solid Tunors; SRS, somatostatin receptor scintigraphy. Strosberg J et al N Engl J Med 2017 276(2): 125-135

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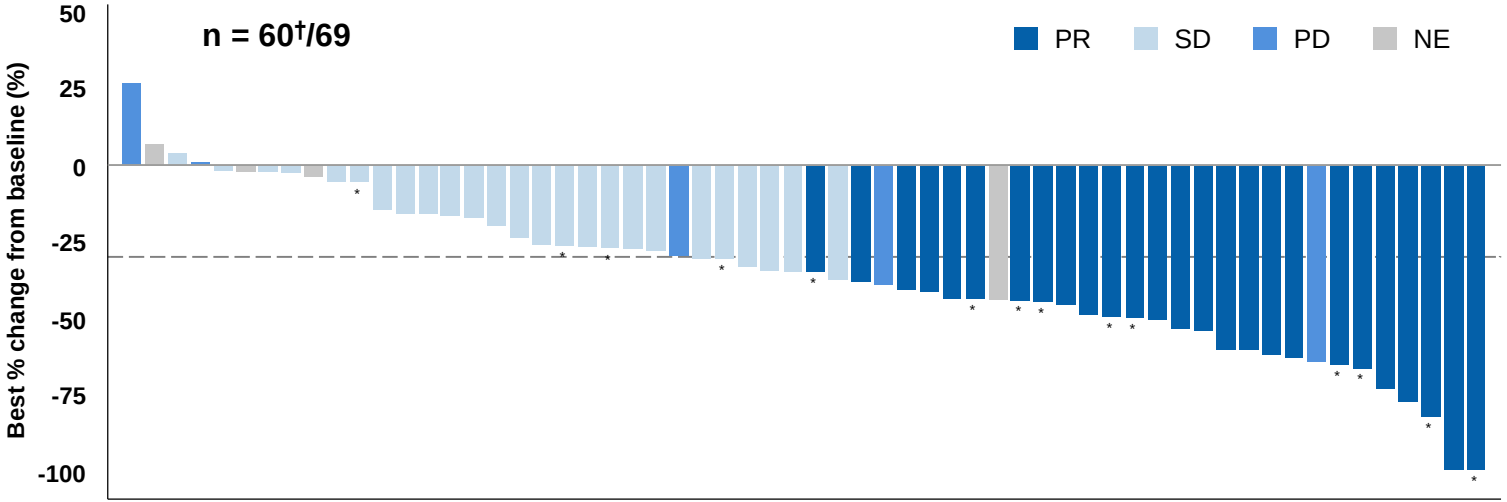
INC280: Tumor response by BIRC (pretreated Cohort 4)

Confirmed ORR by BIRC is 39.1%; most patients show deep responses



*Patients still on treatment

†number of patients with measurable disease at baseline and ≥1 post-baseline assessment

Juergen Wolf. Results of the GEOMETRY mono-1 phase II study for evaluation of the MET inhibitor capmatinib (INC280) in patients with MET exon-14 skipping mutated advanced non-small cell lung cancer. Abstract #LBA52. 2018 European Society of Medical Oncology (ESMO), October 19-23, 2018, Munich, Germany.

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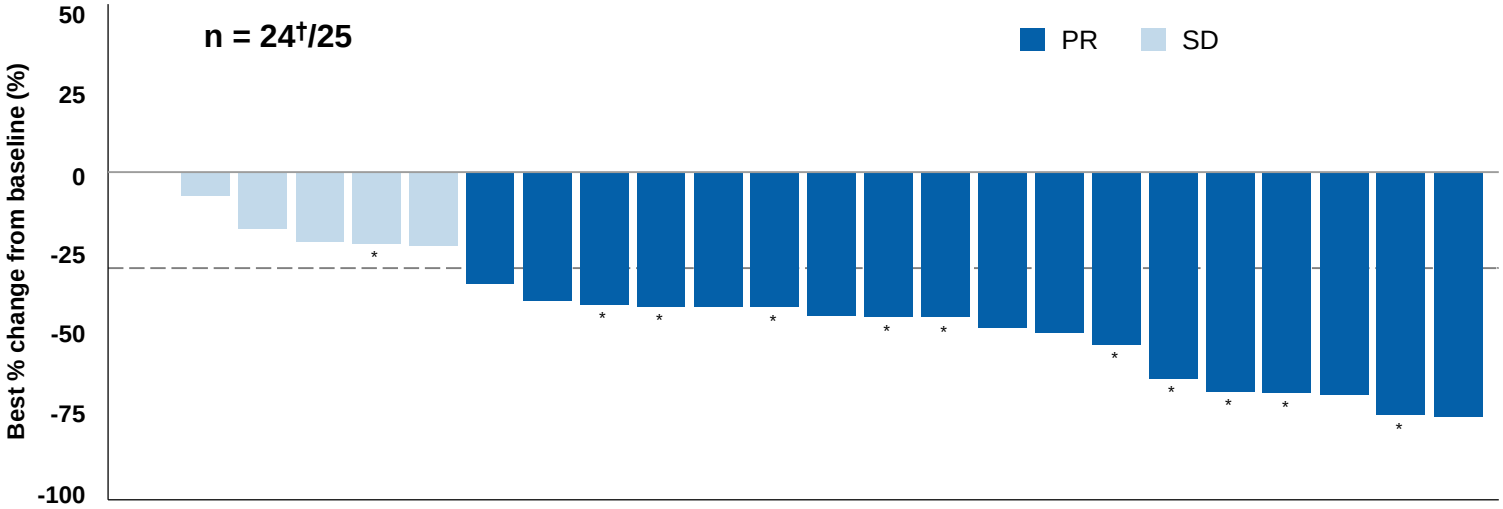
INC280: Tumor response by BIRC (treatment naive Cohort 5b)

Confirmed ORR by BIRC is 72%; deep responses were observed in almost all patients



*Patients still on treatment
†number of patients with measurable disease at baseline and ≥1 post-baseline assessment

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