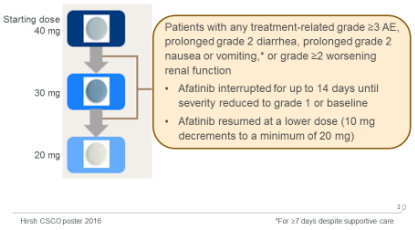
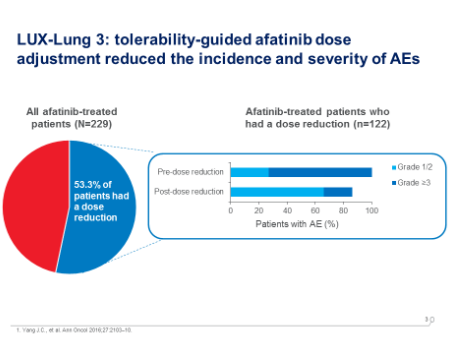
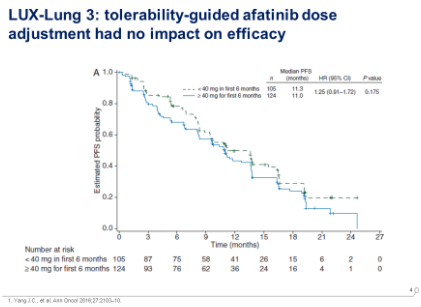
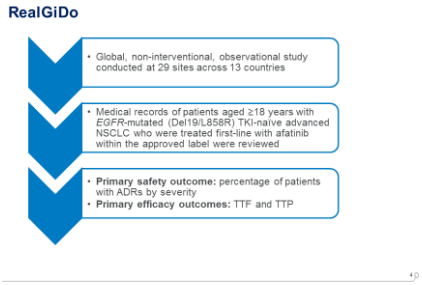
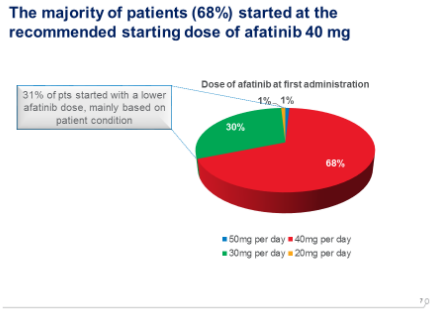
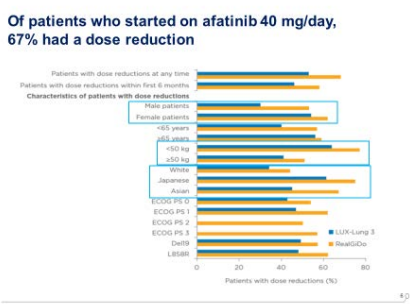
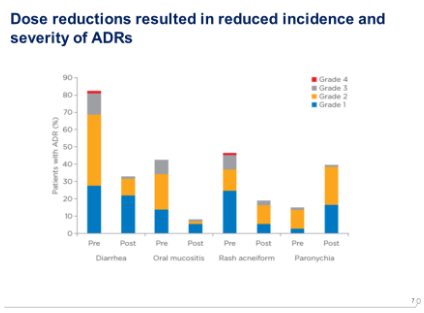
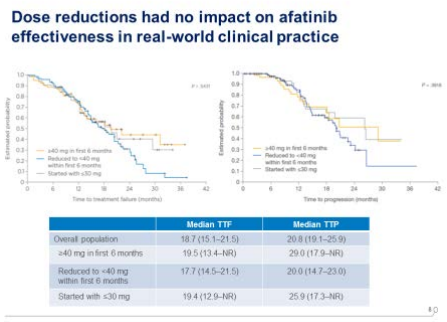
Transcript for video abstract:

Impact of afatinib dose modification on safety and effectiveness in patients with EGFR mutation-positive advanced NSCLC: results from a global real-world study (RealGiDo)
Balazs Halmos

[Title slide] In this article, we report results from the global, non-interventional, observational RealGiDo study, which evaluated the impact on safety and effectiveness of afatinib dose adjustment in the real-world setting.	**[Title slide]** **Impact of afatinib dose modification on safety and effectiveness in patients with *EGFR* mutation-positive advanced NSCLC: results from a global real-world study (RealGiDo)** Balazs Halmos, on behalf of the RealGiDo investigators Department of Oncology, Montefiore/Albert Einstein Cancer Center, Bronx, New York, USA
[Slide 2] Afatinib was approved as front-line therapy for patients with *EGFR* mutation-positive non-small-cell lung cancer on the basis of the phase 3 LUX-Lung 3 and LUX-Lung 6 studies, which demonstrated the superiority of afatinib over chemotherapy. Per the approved label, the recommended starting dose of afatinib is 40 mg/day; however, tolerability dose adjustment is possible, facilitated by the availabity of afatinib in several dose strength formulations. In the case of certain adverse events the afatinib dose can be reduced to 30 mg/day, and further reduced to 20 mg/day if required.	**[Slide 2]** **Afatinib as front-line treatment for *EGFR* mutation-positive NSCLC: dose reduction scheme in LUX-Lung 3 study** 

[Slide 3] Interestingly, post-hoc analysis of LUX-Lung 3 demonstrated that such dose reductions resulted in decreases in the incidence and severity of treatment-related adverse events.	**[Slide 3]** 
[Slide 4] Importantly, these dose reductions had no impact on efficacy, with similar PFS reported for patients who did and those who didn't have dose reductions.	**[Slide 4]** 
[Slide 5] Of course, clinical trial outcomes are not always reflected in the real-world setting as they involve select groups of patients and well-defined, controlled clinical conditions. *[forward animation]* Hence, it was unknown how the LUX-Lung 3 results relate to real-world clinical experience. Consequently, real-world evidence was needed to help physicians guide treatment decisions and management of patients so that they can benefit from afatinib therapy for as long as possible. This need prompted the design of the RealGiDo study.	**[Slide 5]** 

[Slide 6] RealGiDo was a global, non-interventional, observational study conducted at 29 sites across 13 countries. Medical records of adult patients with previously untreated *EGFR*-mutated advanced NSCLC who were treated first-line with afatinib were retrospectively reviewed. The primary safety outcome was the percentage and severity of adverse drug reactions. The primary efficacy outcomes were time to treatment failure and time to progression with afatinib.	**[Slide 6]** 
Slide 7 A total of 228 patients were included, the majority of whom received the recommended starting dose of afatinib 40 mg/day. Approximately one-third of patients received a lower starting dose, mainly for reasons related to the patient's condition	**[Slide 7]** 
Slide 8 Baseline characteristics of the 155 patients who started on Afatinib 40 mg were generally consistent with those reported for afatinib-treated patients in the LUX-Lung 3 trial, but with *[forward animation]* more Del19 patients, likely reflecting treatment guidelines and local practice patterns, and *[forward animation]* *12%* patients with an ECOG performance status of 2/3 were included.	**[Slide 8]** **Patient population** RealGiDo overall population (N=228) / Patients who received afatinib 40 mg: RealGiDo (n=155) / LUX-Lung 3 (N=230) Female, n (%): 138 (60.5) / 89 (57.4) / 147 (64.0) Median age, years (range): 67.0 (32.0–90.0) / 67.0 (32.0–90.0) / 62.0 (28.0–86.0) Median weight, kg (range): 65.0 (37.0–118.0) / 65.0 (37.0–118.0)[a] / 61.1 (12.9)[a] Median BMI, kg/m² (range): 24.2 (13.9–47.3) / 24.6 (13.9–47.3)[a] / 23.9 (4.1)[a] Race, n (%) Asian / White / Other: 100 (43.9) / 96 (42.1) / 3 (1.3) / 74 (47.7) / 57 (37.8) / 2 (1.3) / 166 (72.2) / 61 (26.5) / 3 (1.0) ECOG PS, n (%) 0 / 1 / 2 / 3: 90 (39.5) / 102 (44.7) / 20 (8.8) / 7 (3.1) / 63 (40.7) / 71 (45.8) / 12 (7.7) / 7 (4.5) / 92 (40.0) / 138 (60.0) / 0 / 0 EGFR mutation type, n (%) Del19 / L858R / Other: 176 (78.1) / 49 (21.5) / 0 / 117 (75.5) / 37 (23.6) / 0 / 112 (49.0) / 91 (40.0) / 27 (12.0)
Slide 9 Of patients who started with afatinib 40 mg/day, 67% underwent dose reductions. Dose reductions were mainly due to adverse drug reactions and were more common in *[forward animation]* female, *[forward animation]* East Asian, and *[forward animation]* low body-weight patients.	**[Slide 9]** 

Slide 10 Consistent with results from LUX-Lung 3, dose reductions led to decreases in the incidence and severity of many of the most commonly reported adverse drug reactions, including diarrhea, oral mucositis and rash.	**[Slide 10]** 
Slide 11 Moving on to effectiveness, time to treatment failure and time to progression were consistent regardless of afatinib dose reduction or afatinib starting dose. As shown here, median time to treatment failure and time to progression were similar in patients who dose reduced to less than 40 mg/day within the first 6 months, patients who remained on at least 40 mg/day for the first 6 months, and patients who started with a reduced dose of afatinib.	**[Slide 11]** 
Slide 12 To conclude, these results demonstrate that, consistent with clinical trial evidence, tolerability-guided afatinib dose adjustment in the real-world setting reduced the frequency and intensity of adverse drug reactions without compromising effectiveness. So what do these results mean for real-world clinical practice? Importantly for clinicians, these results support the effectiveness of afatinib as a valuable first-line treatment for patients with *EGFR*-mutation positive NSCLC and highlight that tailoring the afatinib dose based on individual patient characteristics and treatment-related adverse events can help to optimize treatment outcomes in the real-world clinical practice setting.	**[Slide 12]**