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Lung Cancer, non small lung cancer (NSCLC)

This is the short version of onkopedia guidelines for the German-speaking countries. It focuses on algorithms for treatment in different stages with links to the evidence and its appraisal.

Recommendations from the society for diagnosis and therapy of haematological and oncological diseases

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ÖGHO Österreichische Gesellschaft für Hämatologie & Medizinische Onkologie
SSMO SSOM SGMO
SGH+SSH

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Table of contents

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- Guideline
- Conflict of interests

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1 Summary

Lung cancer is the third most frequent malignancy in women and the second most frequent malignancy in men. The median age at diagnosis is between 68 and 70 years. Major risk factor is smoking.

Screening of asymptomatic high-risk persons via low-dose computer tomography (LDCT) can identify lung cancer in early stages. It reduces cancer-specific and overall mortality, especially in women.

Treatment of patients with lung cancer is paradigmatic for modern oncology. NSCLC can now be subdivided in more than a dozen biological entities with individual treatment concepts. Prognosis of patients is determined by stage, histology, immunohistochemistry, sex, ECOG status and comorbidity.

Treatment options include surgery, radiation and systemic treatment, often combined in multimodal concepts. Treatment in early stages and in some patients with advanced stage is curative. For patients in stage IIIB/IV the integration of immune checkpoint and of kinase inhibitors has significantly improved their prognosis.

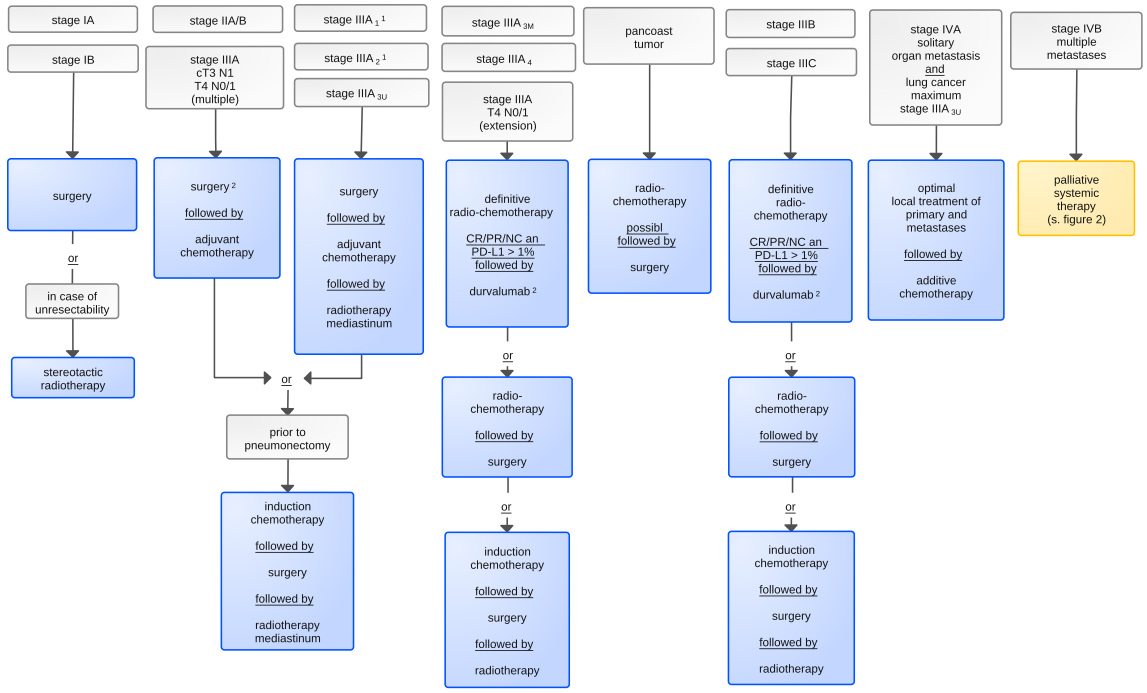
6 Therapy

6.1 Therapeutic algorithm

6.1.1 Primary therapy

Primary therapy is based on the criteria of the 8th lung cancer TNM classification and clinical staging system, see Figure 1.

Figure 1: Algorithm for Primary Therapy



Legend:

curative therapy; palliative therapy;

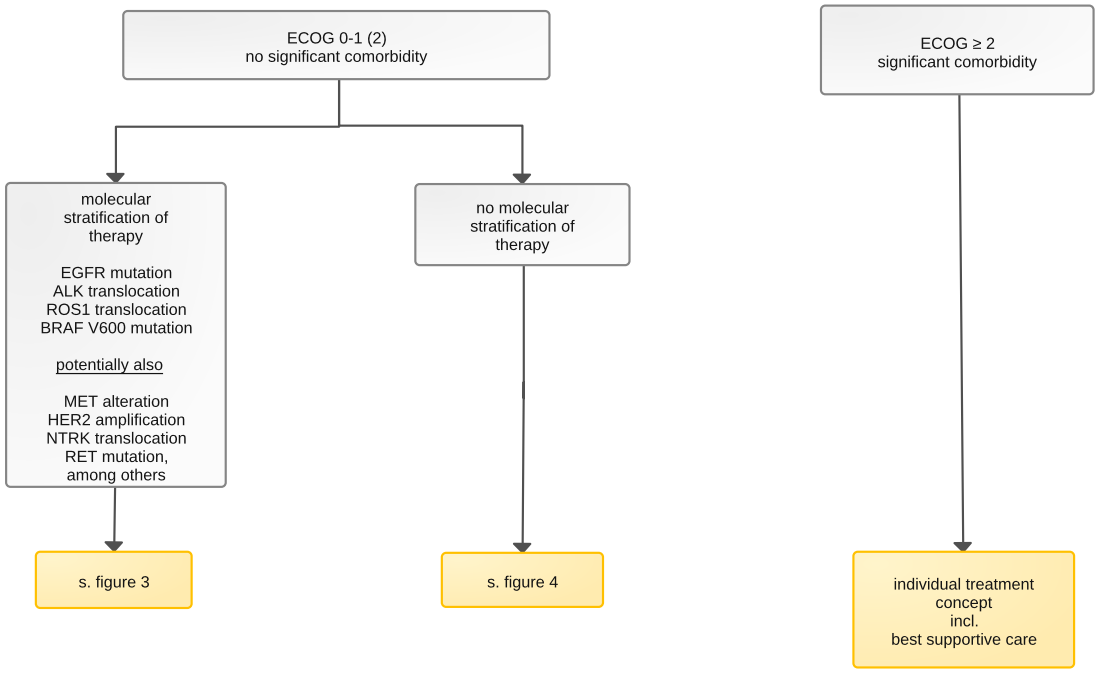
[1] clinical stages;

[2] see figure

6.1.2 Systemic therapy in advanced stages

Recommendations are based on predictive, histological, immunohistochemical and genetic markers, see Figure 2.

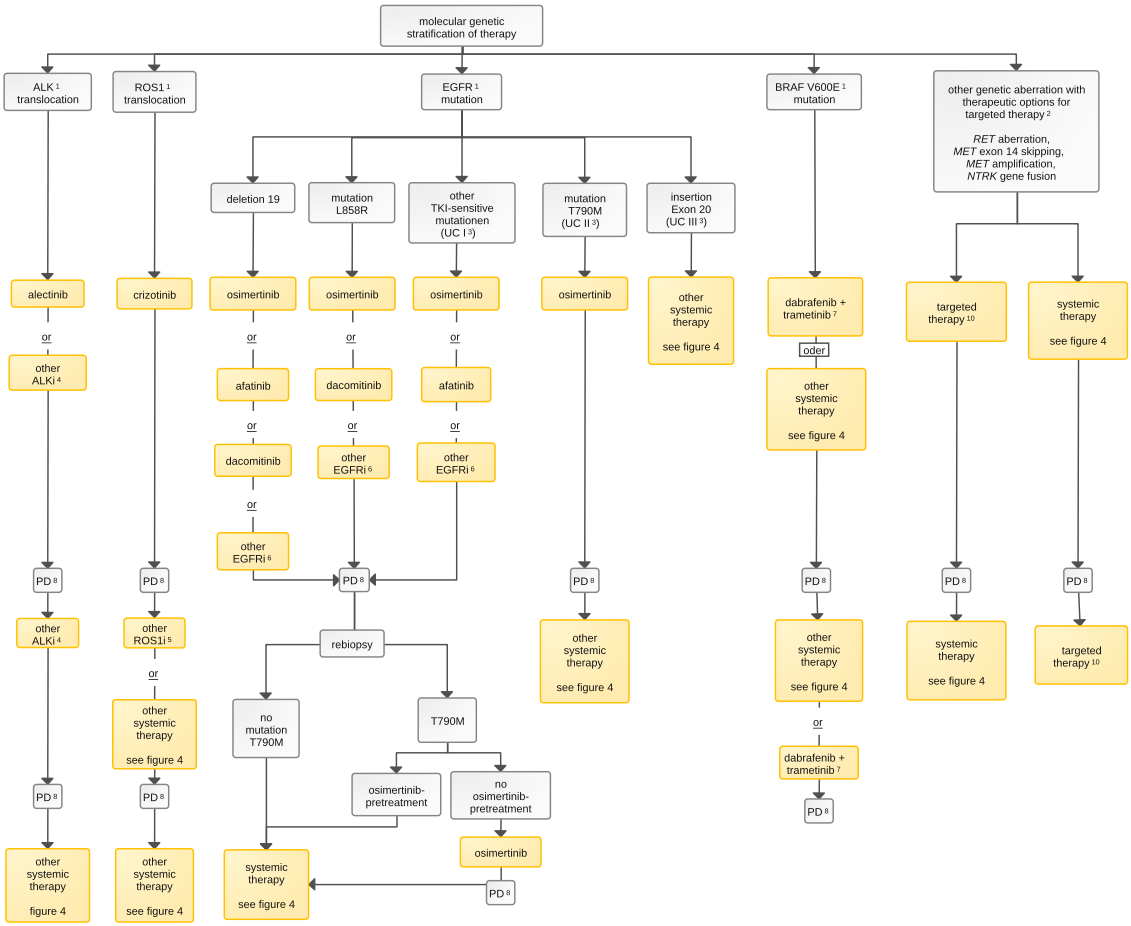
Figure 2: Systemic therapy in advanced stages - overview



6.1.2.1 Molecular genetic stratification of therapy

This chapter contains recommendations for targeted first- and second-line treatment, see Figure 3.

Figure 3: Molecular genetic stratification in advanced stages

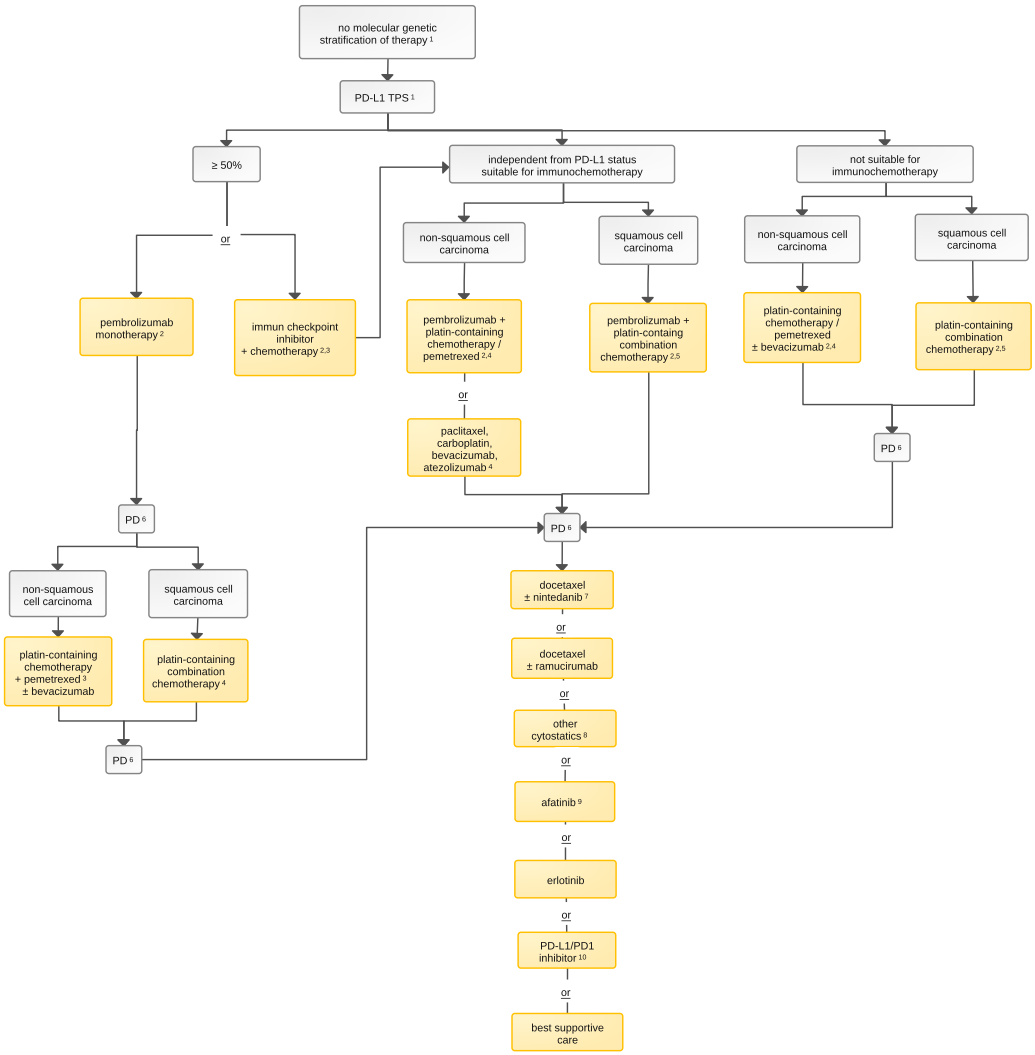


Legend:
[1]no ALK[1]-, ROS1[1]-, EGFR[1]- mutations/translocations, ALK – Anaplastic Lymphoma Kinase, ROS1 – tyrosine protein kinase ROS, EGFR – Epidermal Growth Factor Receptor, BRAFV600E – point mutation in the BRAF gene; [2]other genetic aberrations – RET aberration, c-MET Exon 14 skipping mutation or MET amplification, NTRK fusions; [3]UC – uncommon mutations, UC I – point mutations or duplicatios in EGFR exons 18-21, UCII – mutation T790M in EGFR exon 20 alone or in combination with other mutations, UC III – exon 20 insertions; [4] ALKi – ALK-inhibitor: alectinib, brigatinib, ceritinib, crizotinib, lorlatinib; [5] ROSi – ROS1-inhibitor: ceritinib, crizotinib, cabozantinib, lorlatinib; [6] EGFR-TKI – afatinib, dacomitinib, erlotinib, gefitinib, osimertinib; [7] dabrafenib/trametinib is approved for first and second line therapy by the EU; [8] CR – complete remission, PR – partial remission, SD – stable disease, PD – progressive disease; [9] other systemic therapy, e. g. carboplatin/paclitaxel/ atezolizumab/bevacizumab; [10] see approval status;

6.1.2.2 No molecular genetic stratification of therapy

The majority of patients with NSCLC does not have predictive markers for molecular stratified therapy. Immunochemotherapy has become the standard of care in the first line treatment of these patients, see Figure 4.

Figure 4: No molecular genetic stratification advanced stages



Legend:
[1] PD-L1 TPS – expression of PD-L1 on tumor cells, quantified by the Tumor Progression Score (TPS); [2] suitable for immunotherapy with no significant contraindications; [3] combination of an immune checkpoint inhibitor and histology-stratified chemotherapy; [4] combination of cis- or carboplatin and pemetrexed; [5] combination of carboplatin and paclitaxel or nab paclitaxel; [6] CR – complete remission, PR – partial remission, SD – stable disease, PD – progressive disease; [7] nintedanib only in adenocarcinoma; [8] third generation cytostatic drugs: gemcitabine, pemetrexed, vinorelbine; pemetrexed only in non-squamous cell carcinoma; [9] afatinib only in squamous cell carcinoma; [10] PD-1/PD-L1 inhibitor: atezolizumab (independent of PD-L1 expression), nivolumab (independent of PD-L1 expression), pembrolizumab (only with TPS ≥1%); efficacy has not been demonstrated in patients who received immune checkpoint inhibitors in first line;

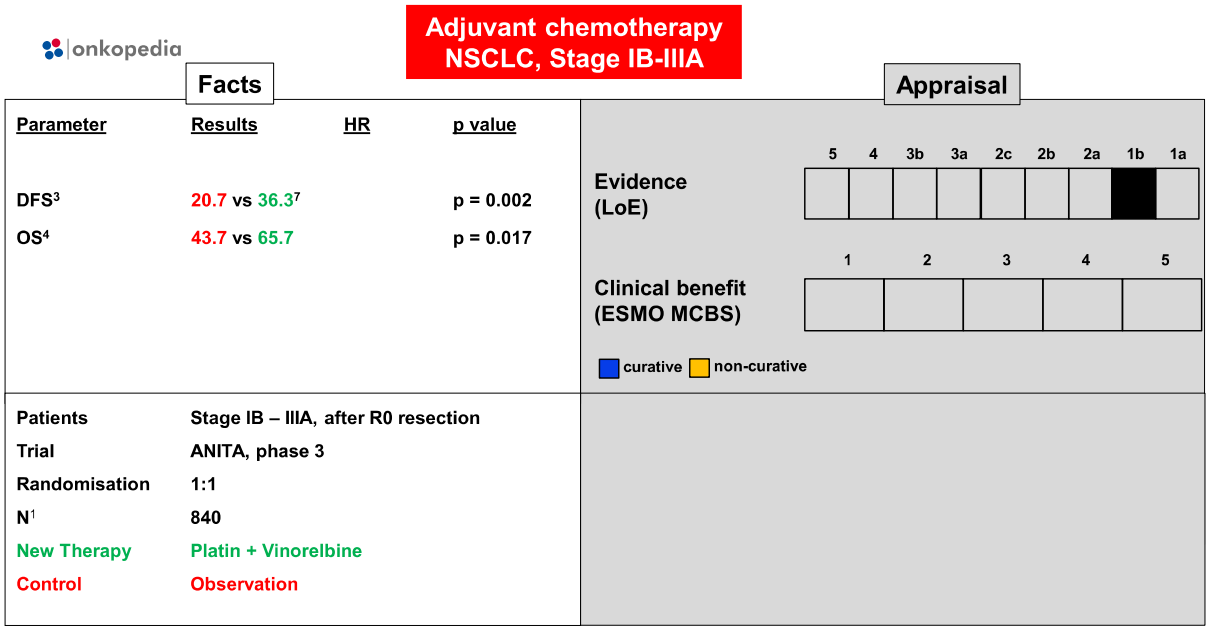
6.2 Facts and Appraisal

6.2.1 Adjuvant therapy

6.2.1.1 Adjuvant chemotherapy

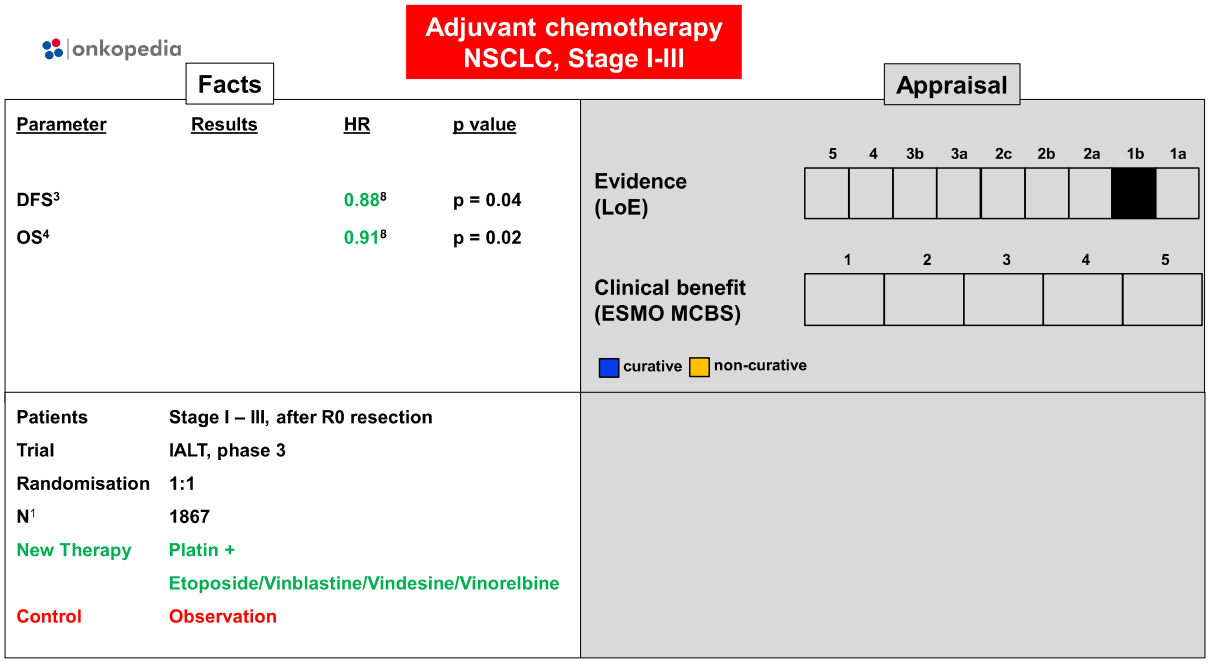
Adjuvant chemotherapy is recommended in patients with stages II-IIIA after surgical R0 resection. Data are summarized in Figure 5 and Figure 6.

Figure 5: Adjuvant chemotherapy in NSCLC (ANITA trial)



Legend:
[1] N - number of patients; [3] DFS – disease-free survival rate after 76 months, in %; [4] OS – overall survival rate after 76 months, in %; [7] results for control, results for new therapy; [8] hazard ratio for new therapy;
Publication: DOI:10.1016/S1470-2045(06)70804-X

Figure 6: Adjuvant chemotherapy in NSCLC (IALT trial);



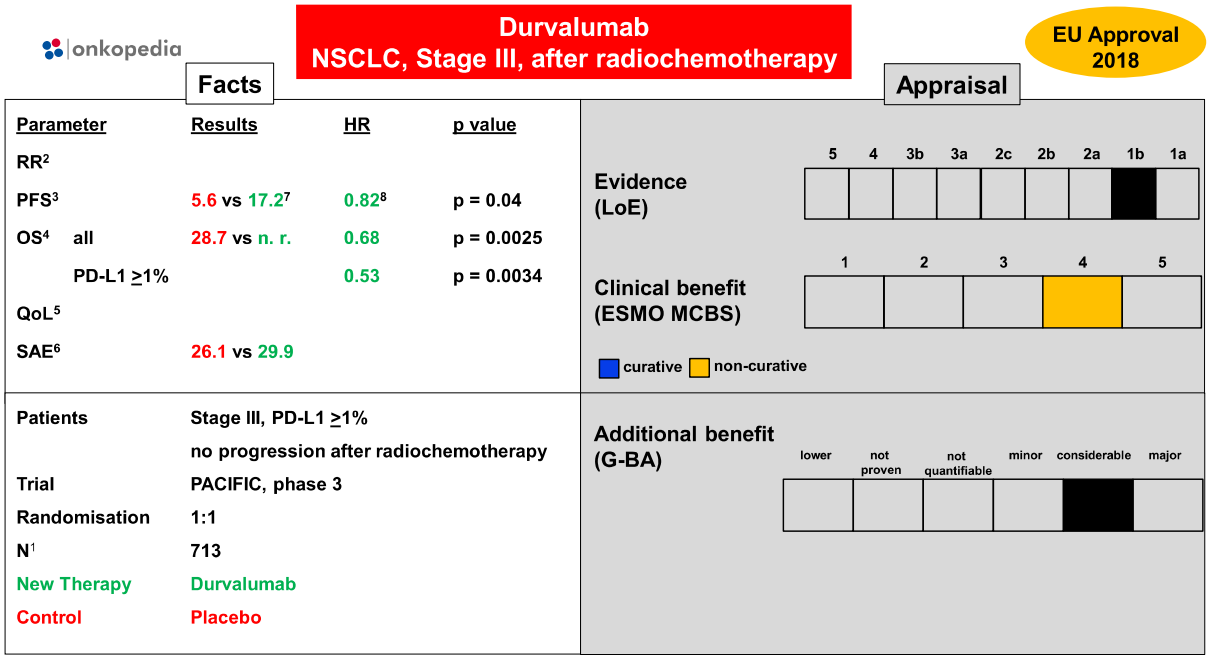
Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] DFS – disease-free survival; [4] OS – overall survival; [8] hazard ratio for new therapy;
Publication: DOI:10.1200/JCO.2009.23.2272

6.2.1.2 Adjuvant immunotherapy

6.2.1.2.1 Durvalumab, Stage III, after radiochemotherapy

Data are summarized in Figure 7.

Figure 7: Durvalumab in NSCLC, Stage III, after radiochemotherapy



Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy;
Publication DOI:10.1056/NEJMoa1709937; DOI:10.1056/NEJMoa1809697

6.2.2 Advanced stages

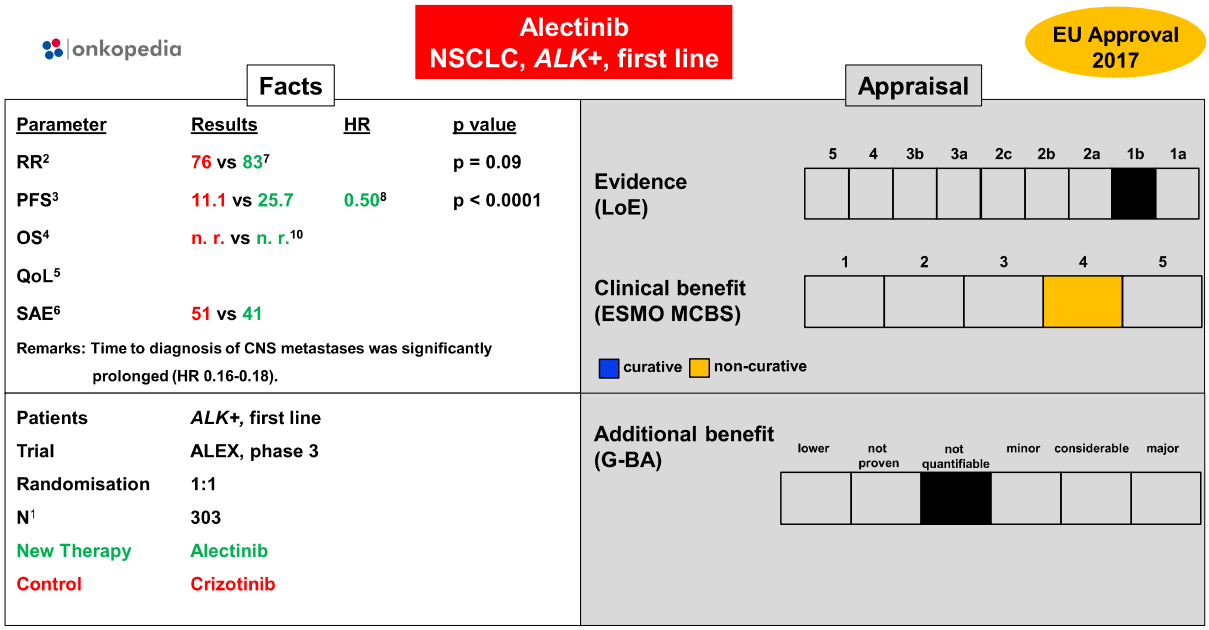
6.2.2.1 Molecular genetic stratification

6.2.2.1.1 ALK inhibitors

6.2.2.1.1.1 First line, molecular genetic stratification

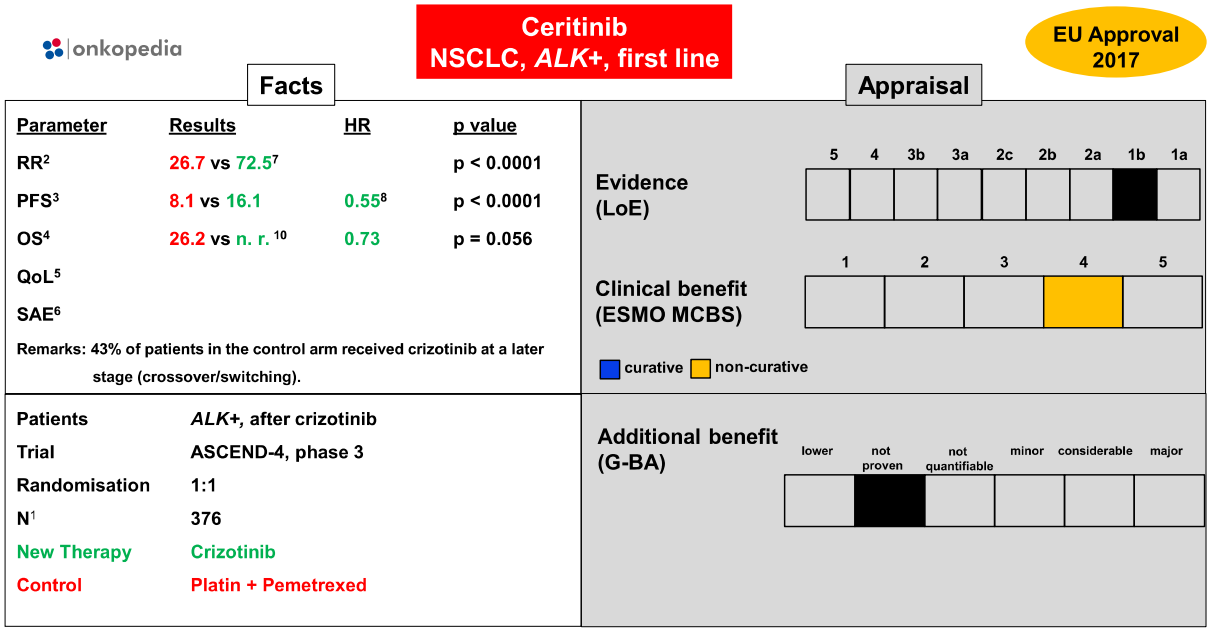
Data are summarized in Figure 8, Figure 9 and Figure 10.

Figure 8: Alectinib in ALK+ NSCLC, first line



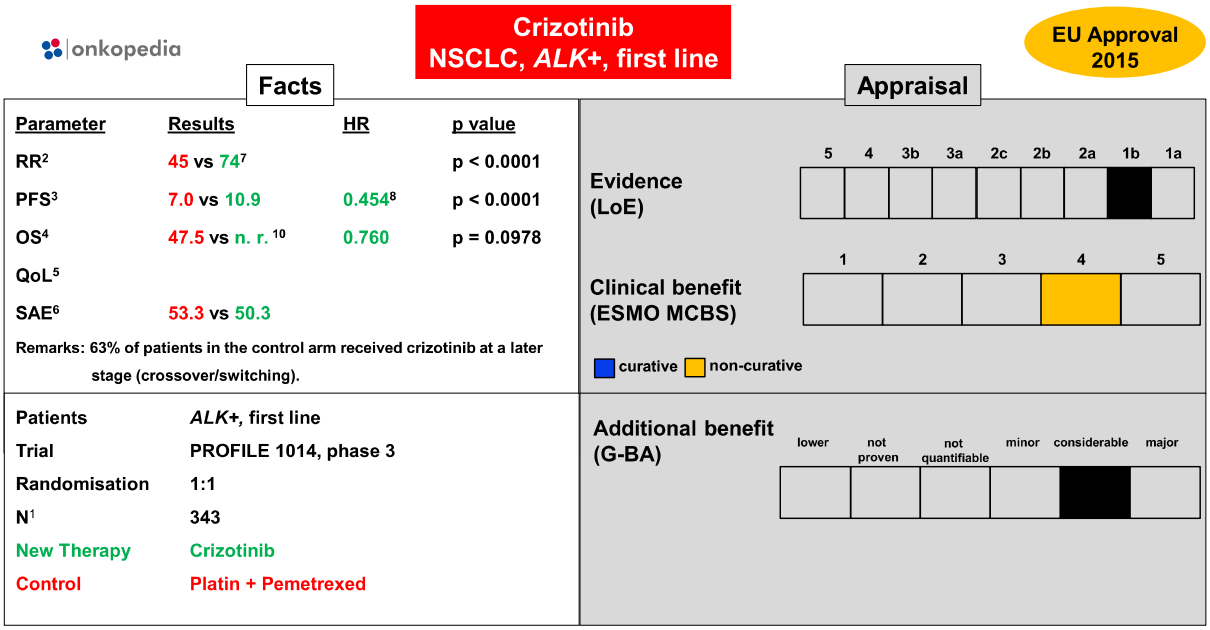
Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS - overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [9] n. s. - not significant; [10] n. r. – median not reached;
Publication: DOI:10.1056/NEJMoa1704795

Figure 9: Ceritinib in NSCLC, ALK+, first line



Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS - overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [9] n. s. - not significant; [10] n. r. – median not reached;
Publication: DOI:10.1016/S0140-6736(17)30123-X

Figure 10: Crizotinib in NSCLC, ALK+, first line

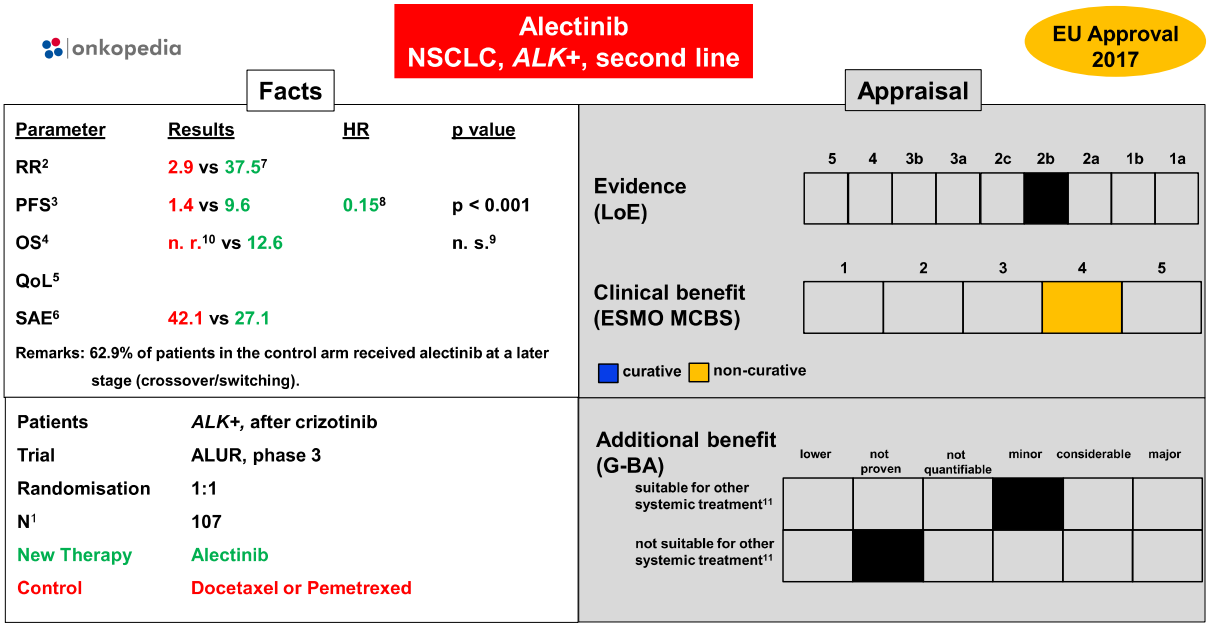


Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS - overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [9] n. s. - not significant; [10] n. r. – median not reached;
Publication: DOI:10.1056/NEJMoa1408440; DOI:10.1200/JCO.2017.77.4794

6.2.2.1.1.2 Second line, molecular genetic stratification

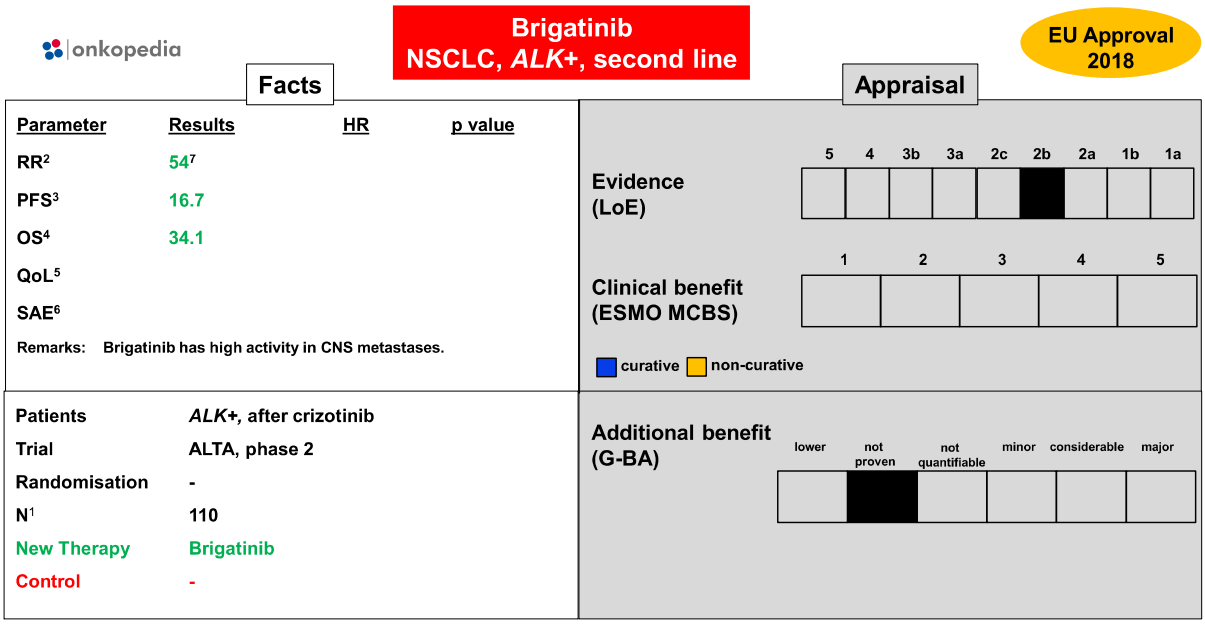
Data are summarized in Figure 11, Figure 12, Figure 13 and Figure 14.

Figure 11: Alectinib in ALK+ NSCLC, second line



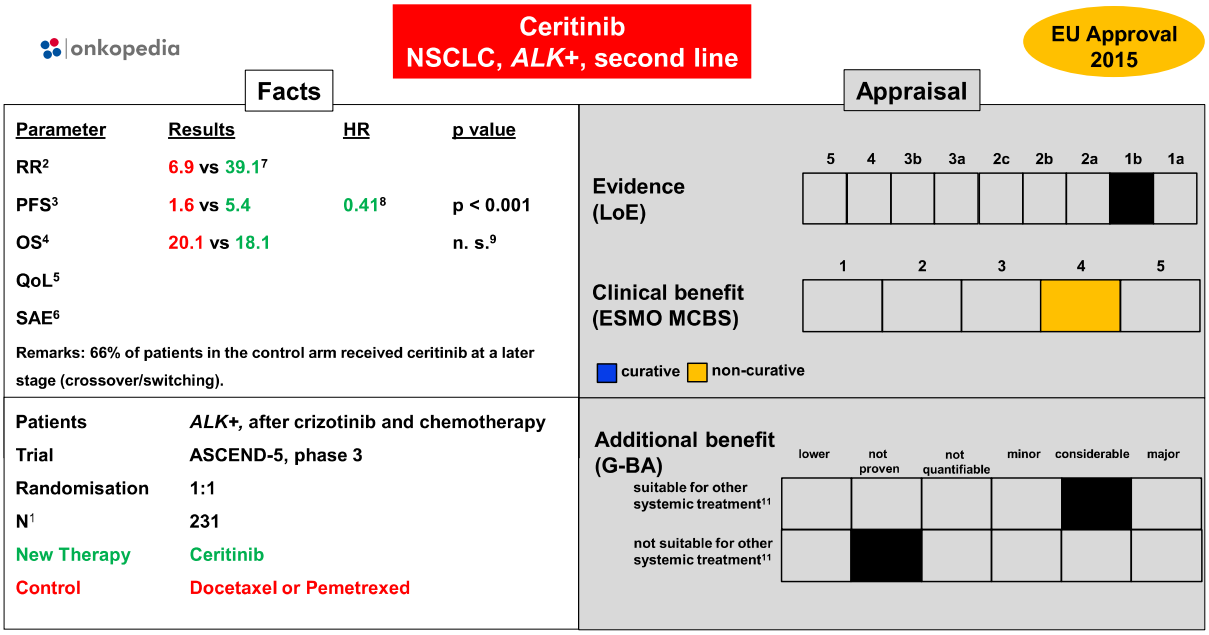
Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS - overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [9] n. s. - not significant; [10] n. r. – median not reached; [11] pemetrexed. docetaxel or ceritinib
Publication: DOI:10.1093/annonc/mdy121

Figure 12: Brigatinib in NSCLC, ALK+, second line



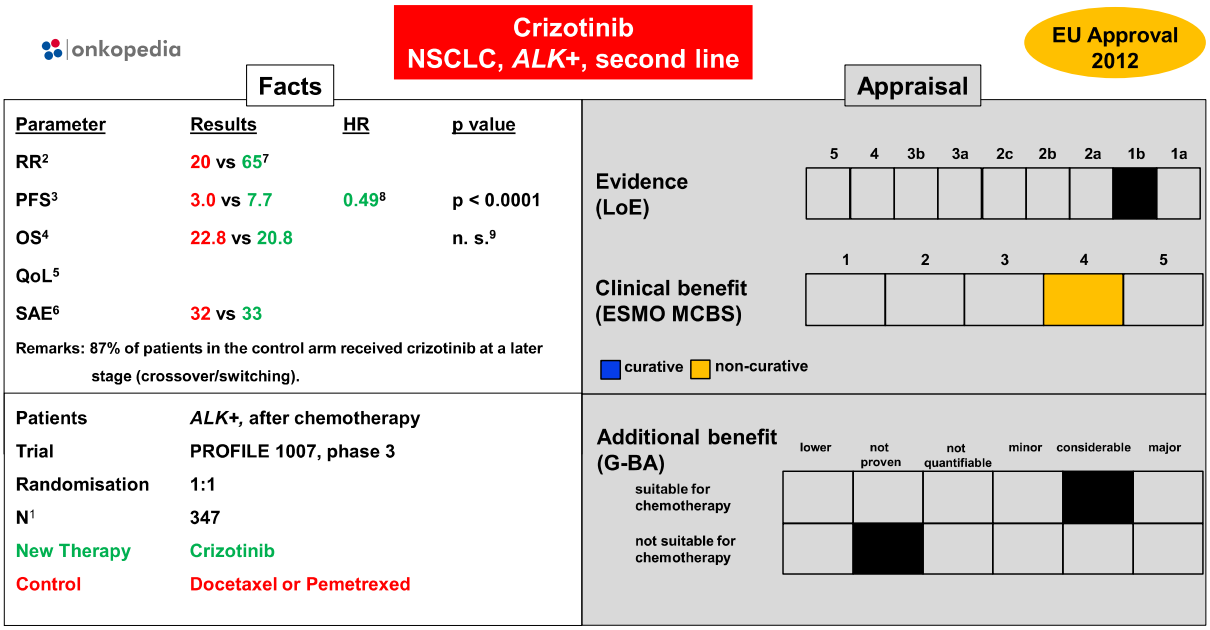
Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS - overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy;
Publication: DOI:10.1200/JCO.2016.71.5904

Figure 13: Ceritinib in NSCLC, ALK+, second line



Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS - overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [9] n. s. - not significant; [11] pemetrexed or docetaxel
Publication: DOI:10.1016/S1470-2045(17)30339-X

Figure 14: Crizotinib in NSCLC, ALK+, second line

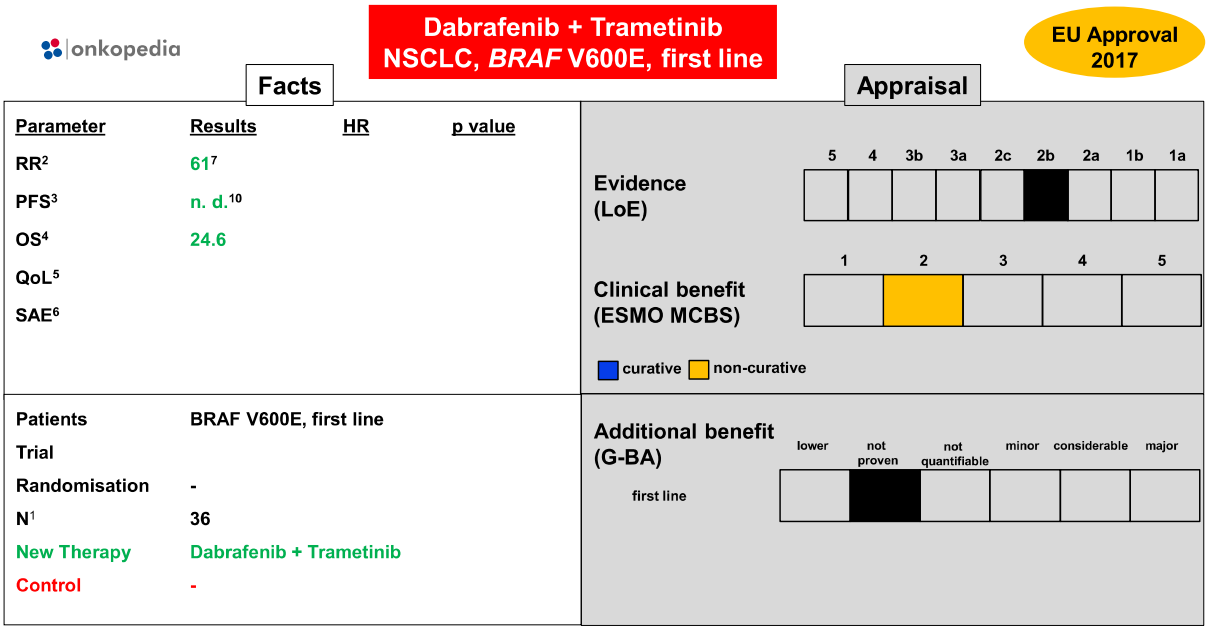


Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS - overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [9] n. s. - not significant;
Publication: DOI:10.1056/NEJMoa1214886

6.2.2.1.2 BRAF inhibitors, first and second line

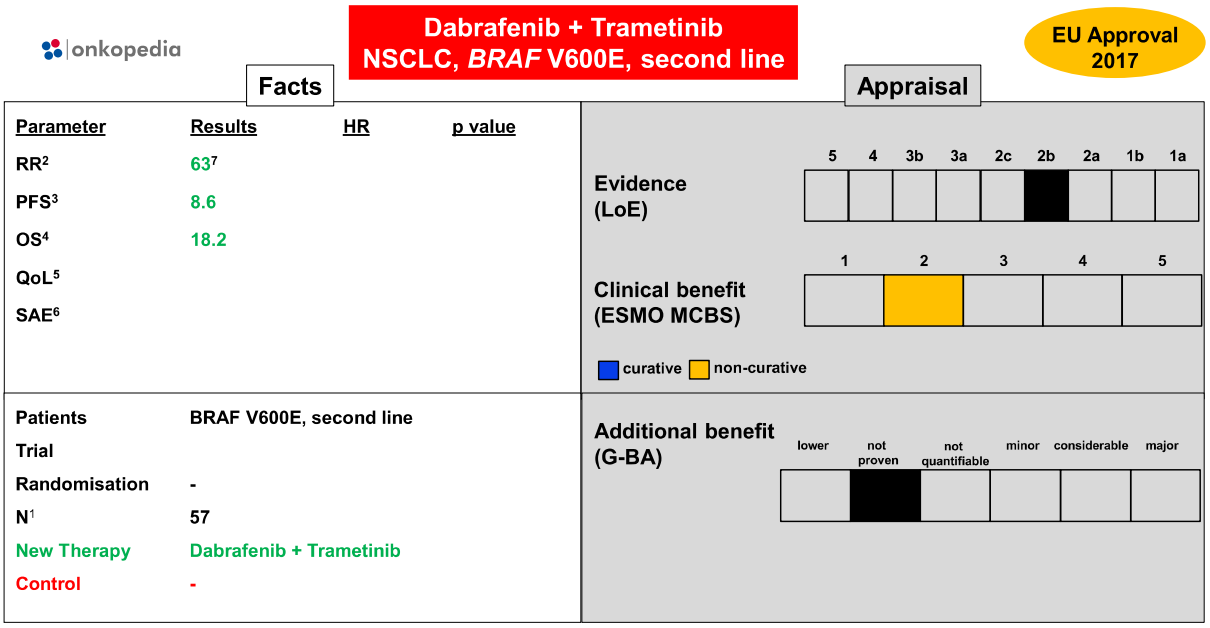
Data are summarized in Figure 15 and Figure 16.

Figure 15: Dabrafenib + Trametinib in NSCLC, BRAF V600E, first line



Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [9] n. s. - not significant; [10] n. d. - not determined;
Publication: DOI:10.1016/S1470-2045(17)30679-4

Figure 16: Dabrafenib + Trametinib in NSCLC, BRAF V600E, second line



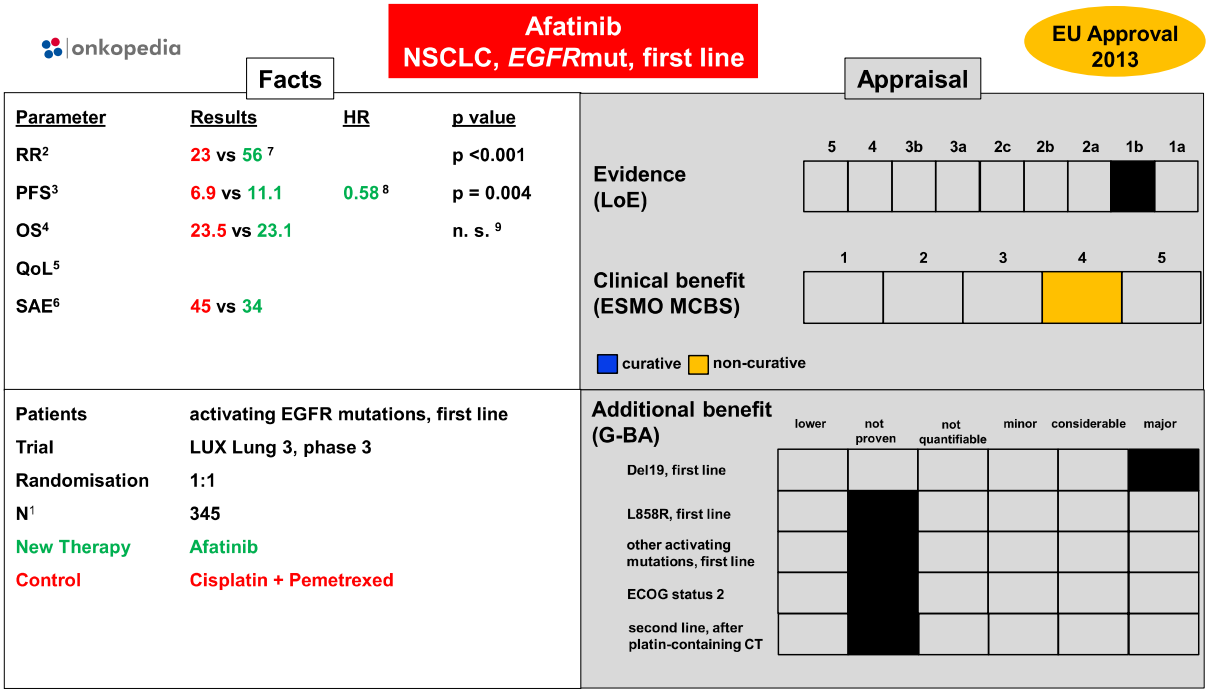
Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [9] n. s. - not significant; [10] n. d. - not determined;
Publication: DOI:10.1016/S1470-2045(16)30146-2

6.2.2.1.3 EGFR inhibitors

6.2.2.1.3.1 First line, EGFR inhibitors

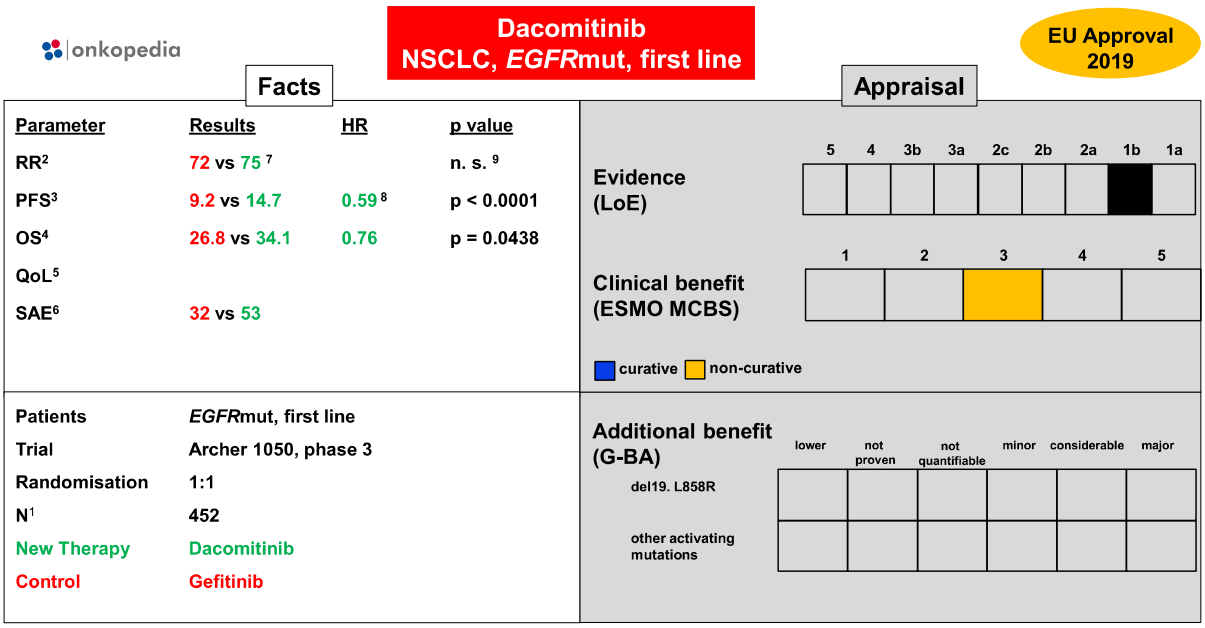
Data are summarized in Figure 17, Figure 18, Figure 19, Figure 20, Figure 21 and Figure 22.

Figure 17: Afatinib in EGFRmutated NSCLC, first line



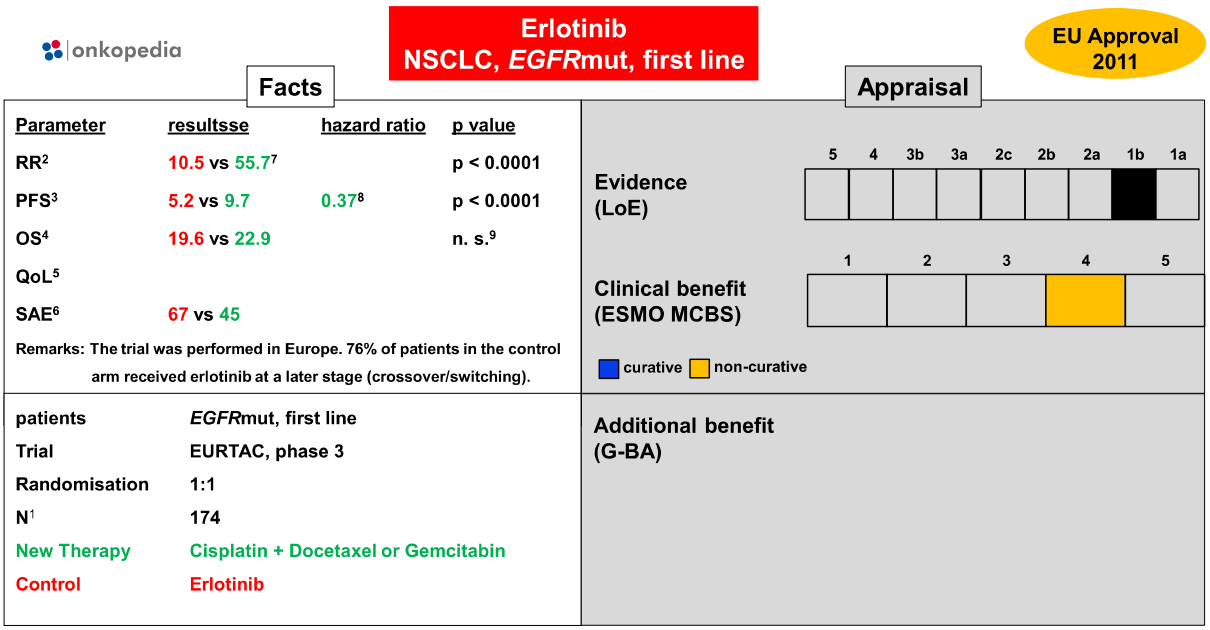
Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [9] n. s. - not significant; [10] n. d. - not determined; CT - chemotherapy
Publication: DOI:10.1016/S1470-2045(13)70604-1; DOI:10.1016/S1470-2045(15)00026-1; DOI:10.1016/j.cllc.2018.03.009

Figure 18: Dacomitinib in NSCLC, EGFRmut, first line



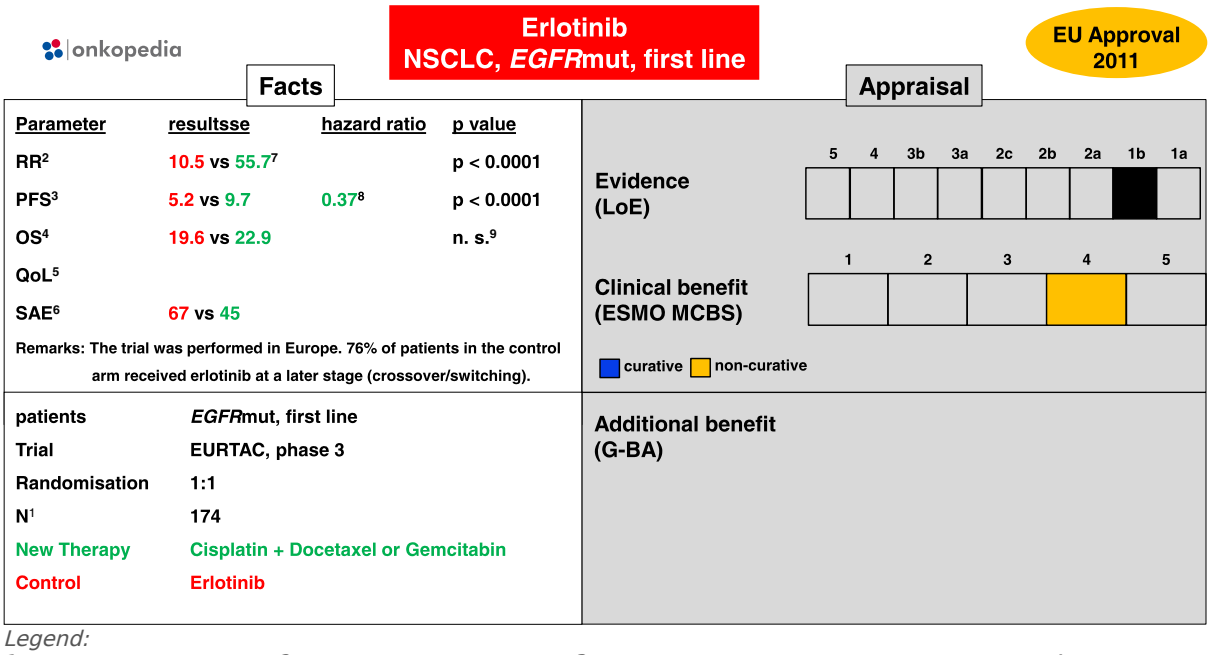
Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [9] n. s. - not significant; [10] n. d. - not determined;
Publication: DOI:10.1016/S1470-2045(17)30608-3; DOI:10.1200/JCO.2018.78.7994

Figure 19: Erlotinib in NSCLC, EGFRmut, first line (OPTIMAL)



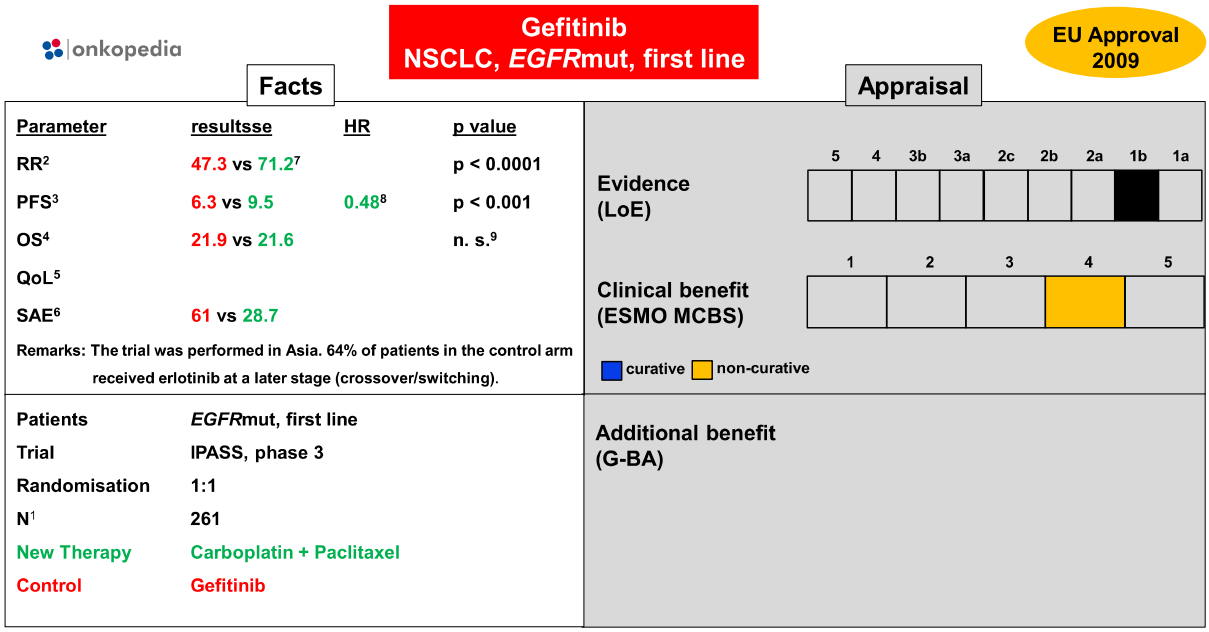
Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [9] n. s. - not significant; [10] n. d. - not determined;
Publication: DOI:10.1016/S1470-2045(11)70393-X

Figure 20: Erlotinib in NSCLC, EGFRmut, first line (EURTAC)



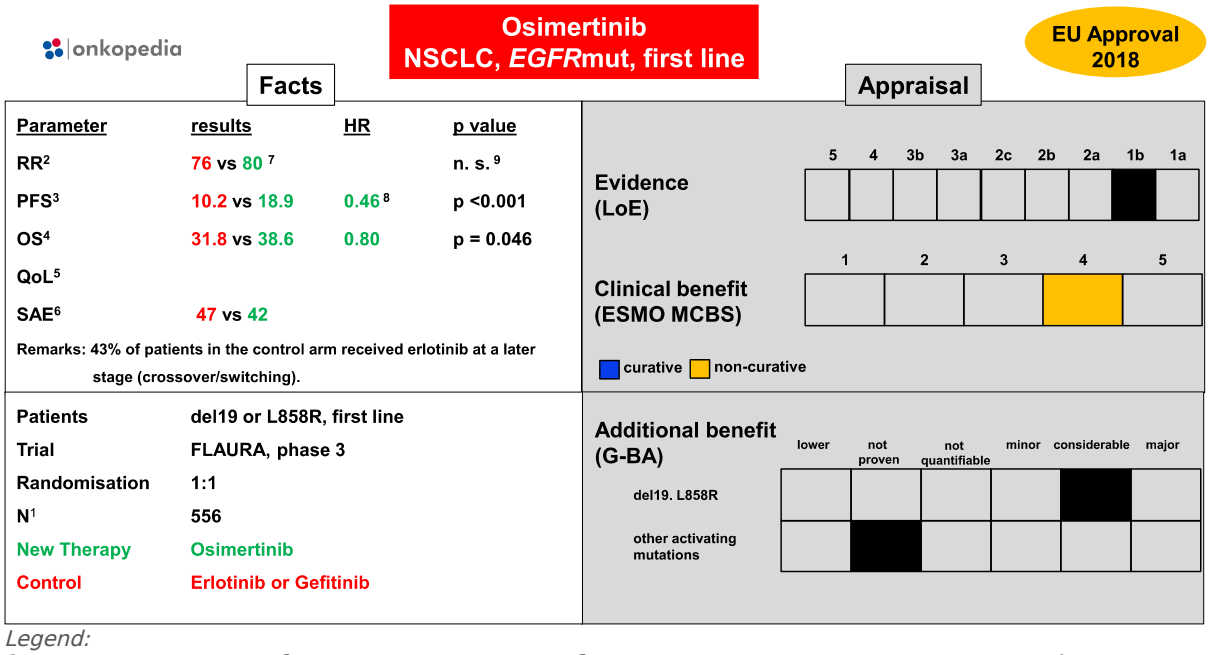
Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [9] n. s. - not significant; [10] n. d. - not determined;
Publication: DOI:10.1016/S1470-2045(11)70393-X

Figure 21: Gefitinib in NSCLC, EGFRmut, first line



Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [9] n. s. - not significant; [10] n. d. - not determined;
Publication: DOI:10.1056/NEJMoa0810699; DOI:10.1200/JCO.2010.33.4235

Figure 22: Osimertinib in NSCLC, EGFRmut, first line

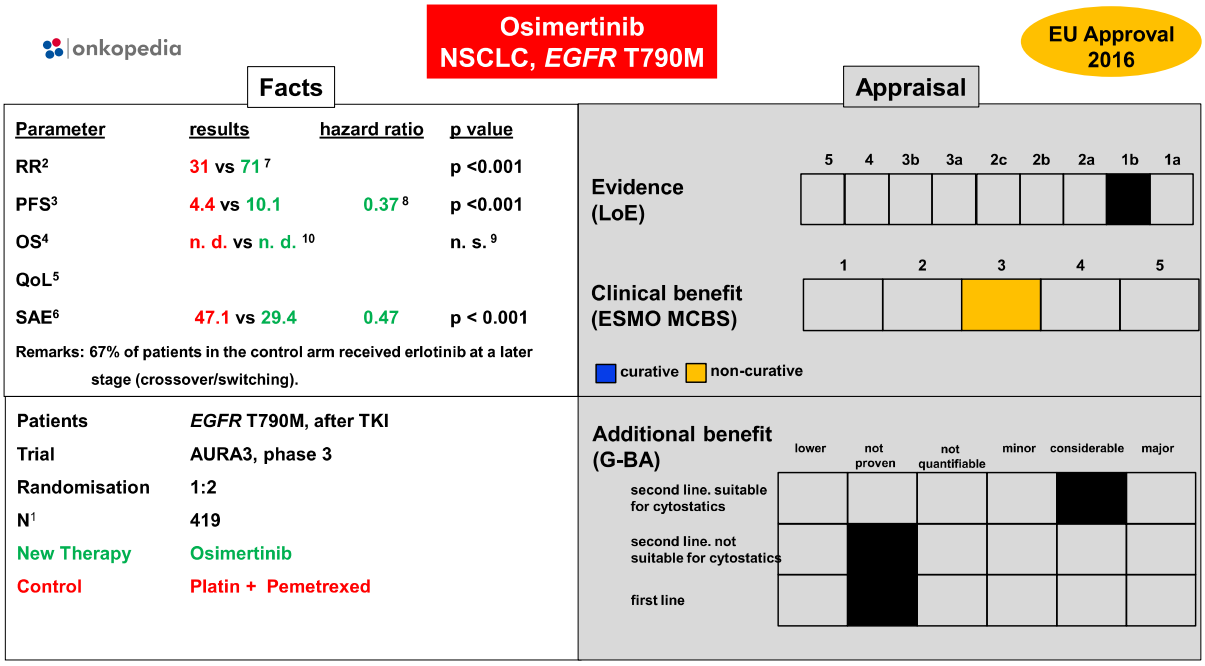


Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [9] n. s. - not significant; [10] n. d. - not determined;
Publication: DOI:10.1056/NEJMoa1713137; DOI:10.1056/NEJMoa1913662

6.2.2.1.3.2 Second line, EGFR T790M

Data are summarized in Figure 23.

Figure 23: Osimertinib in NSCLC, EGFR T790M



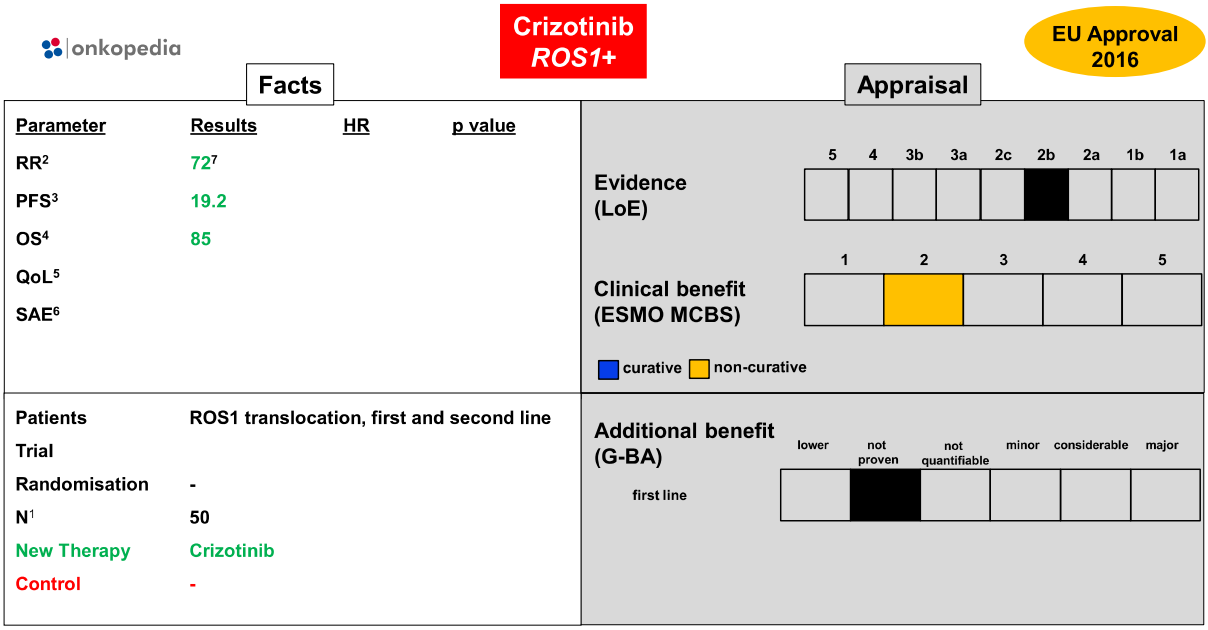
Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [9] n. s. - not significant; [10] n. d. - not determined;
Publication: DOI:10.1056/NEJMoa1411817; DOI:10.1056/NEJMoa1612674

6.2.2.1.4 ROS1 inhibitors

6.2.2.1.4.1 Crizotinib, ROS1 inhibitors

Data are summarized in Figure 24.

Figure 24: Crizotinib in NSCLC, ROS1+



Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival rate after 12 months, in%; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for new therapy; [8] hazard ratio for new therapy;
Publication: DOI:10.1056/NEJMoa1406766

6.2.2.1.4.2 Others, ROS1 inhibitors

Other kinase inhibitors like ceritinib, cabozantinib, entrectinib and lorlatinib show effectivity in *ROS-1* translocated NSCLC, but are not approved in the EU.

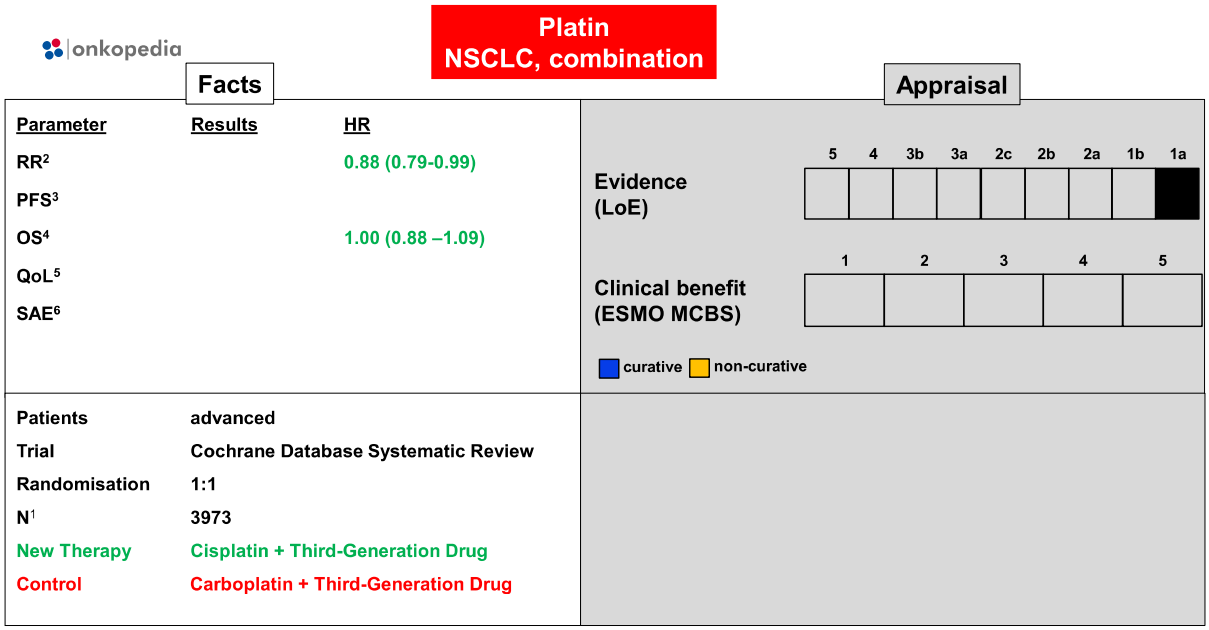
6.2.2.2 No molecular genetic stratification

6.2.2.2.1 Chemotherapy

6.2.2.2.1.1 First line, no molecular genetic stratification

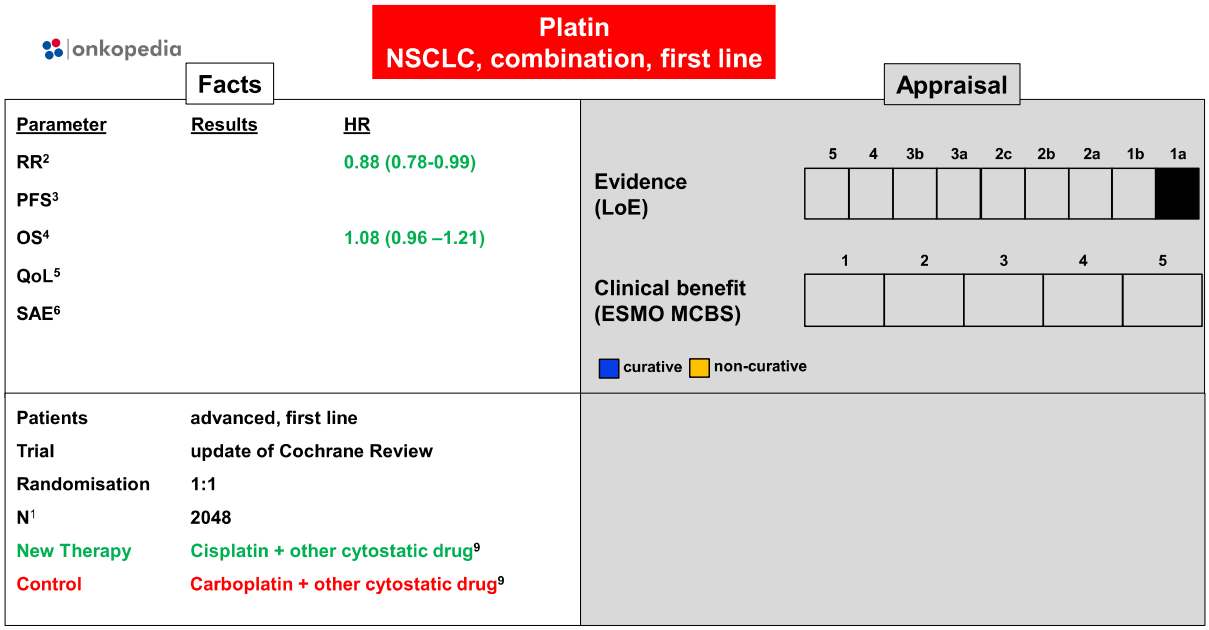
Cytostatic drugs are the backbone of systemic therapy in these patients. Data on the selection of platin derivates are summarized in Figure 25 and Figure 26, data on pemetrexed in Figure 27.

Figure 25: Platin derivates in NSCLC, advanced stages



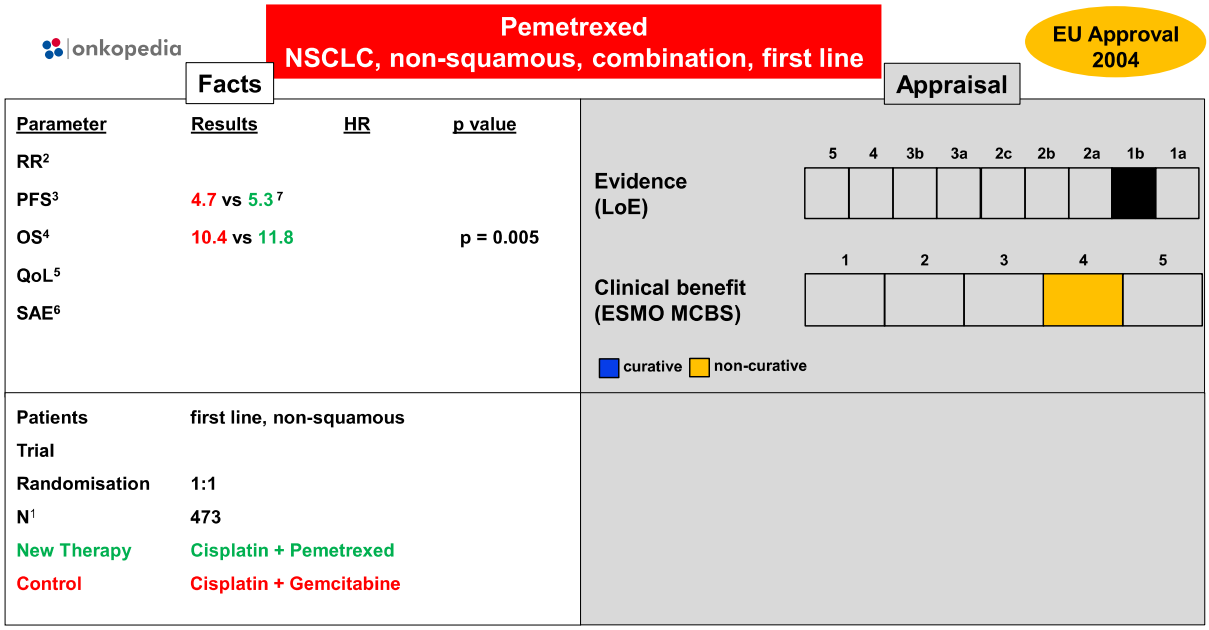
Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy (confidence interval);
Publication: DOI:10.1002/14651858.CD009256.pub2

Figure 26: Platin derivates in NSCLC, first line



Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months, in %; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [8] hazard ratio for new therapy (confidence interval); [9] gemcitabine, vinorelbine, docetaxel, paclitaxel, irinotecan, or pemetrexed;
Publication: DOI:10.1016/j.lungcan.2019.07.010

Figure 27: Pemetrexed in NSCLC, first line

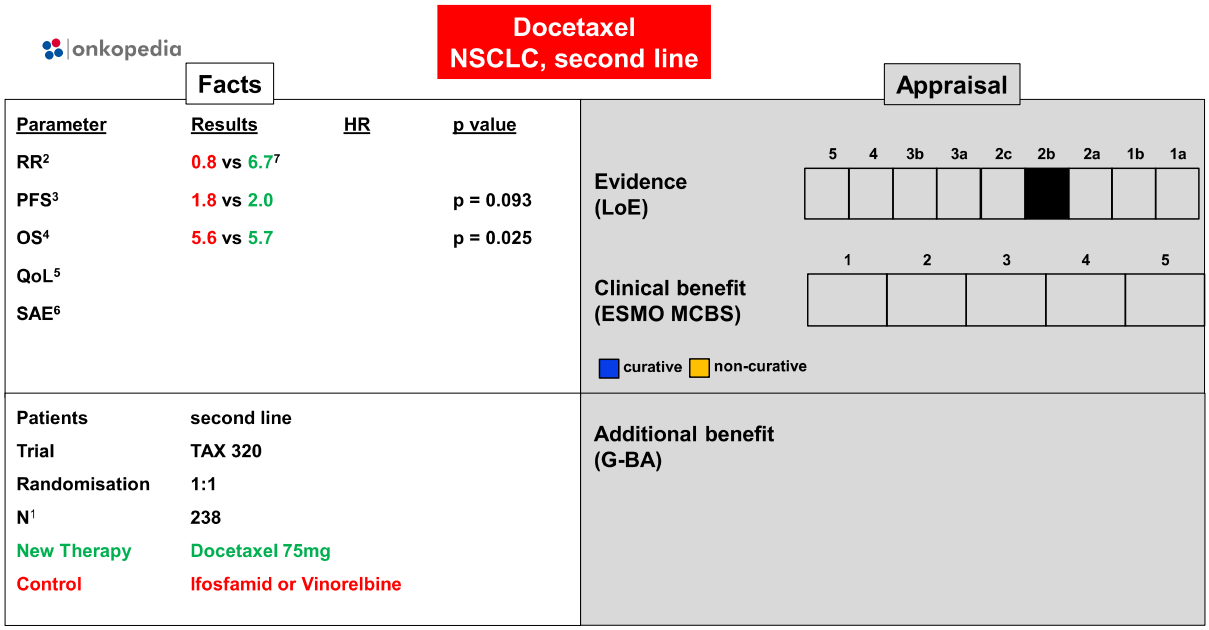


Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months, in %; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy;
Publication: DOI:10.1200/JCO.2007.15.0375

6.2.2.2.1.2 Second line, no molecular genetic stratification

Data on docetaxel are summarized in Figure 28.

Figure 28: Docetaxel in NSCLC, second line



Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months, in %; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy;
Publication: DOI:10.1200/JCO.2000.18.12.2354

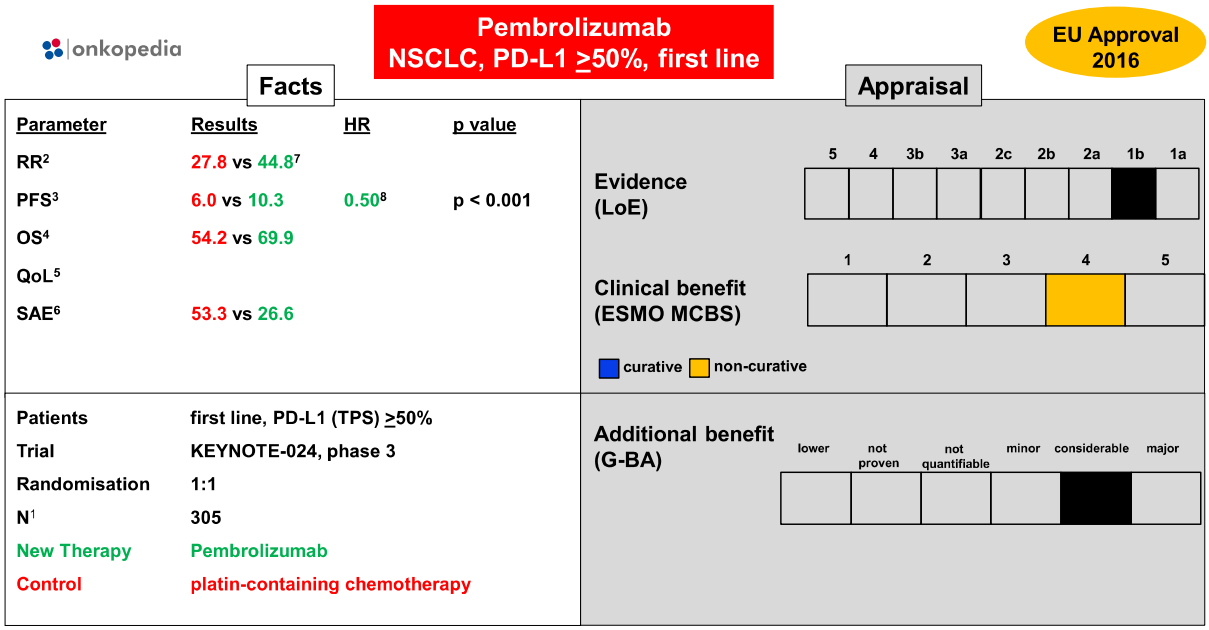
6.2.2.2.2 Immunotherapy

Immune checkpoint inhibitors are approved as monotherapy and in combination with chemotherapy.

6.2.2.2.2.1 First line, monotherapy

Data are summarized in Figure 29.

Figure 29: Pembrolizumab in NSCLC, PD-L1 ≥%, first line

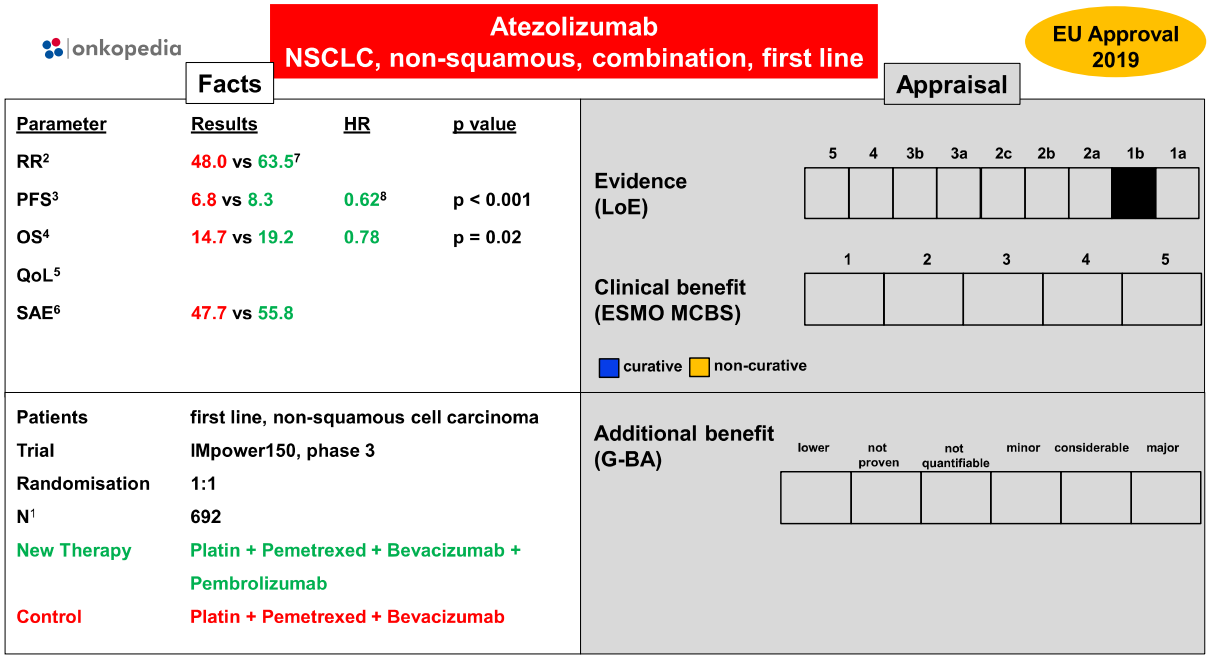


Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months, in %; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy;
Publication: DOI:10.1056/NEJMoa1606774

6.2.2.2.2 First line, combination therapy

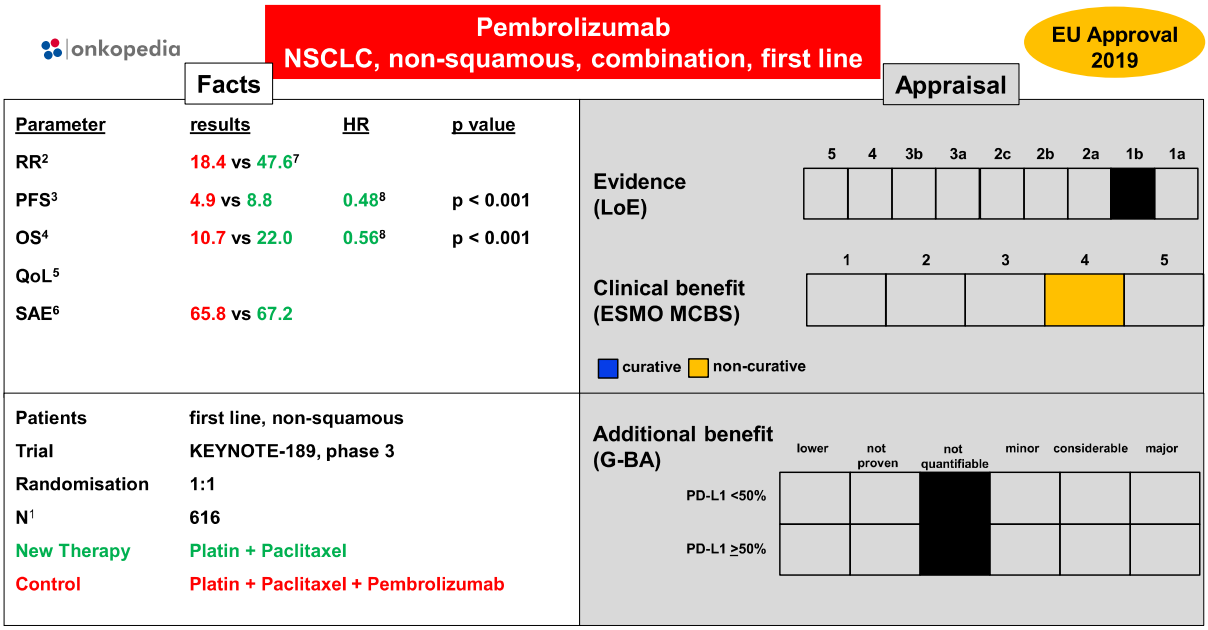
Data are summarized in Figure 30, Figure 31 and Figure 32.

Figure 30: Atezolizumab in NSCLC, non-squamous, combination, first line



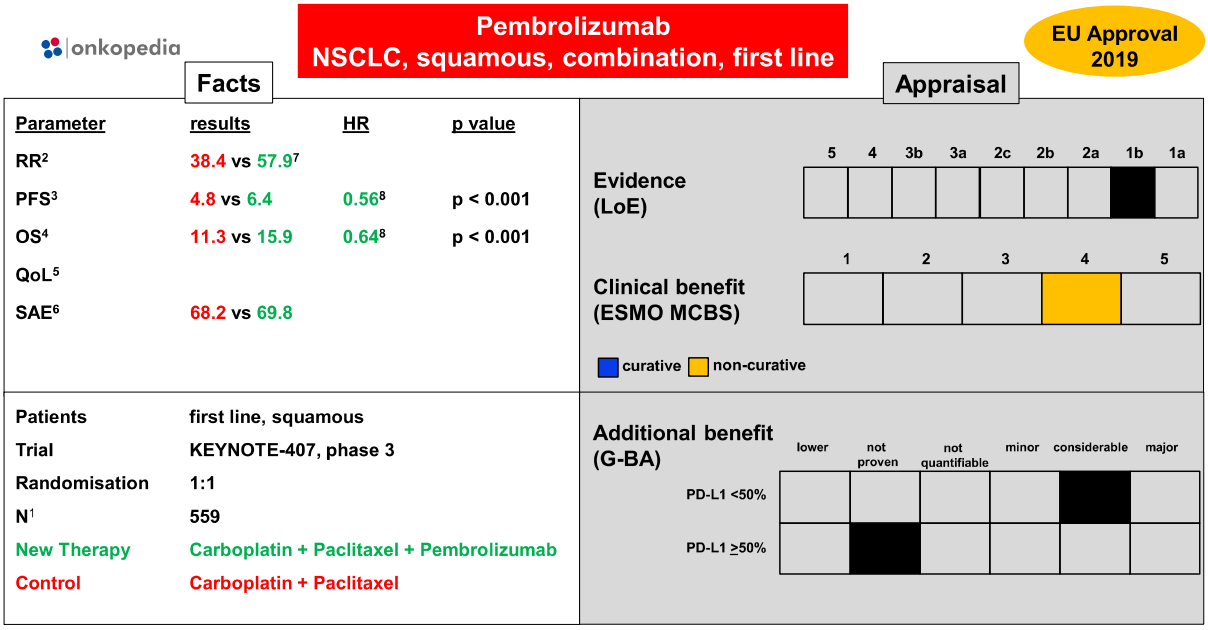
Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months, in %; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy;
Publication: DOI:10.1056/NEJMoa1716948

Figure 31: Pembrolizumab in NSCLC, non-squamous, combination, first line



Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months, in %; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy;
Publication: DOI:10.1056/NEJMoa1801005

Figure 32: Pembrolizumab in NSCLC, squamous, combination, first line

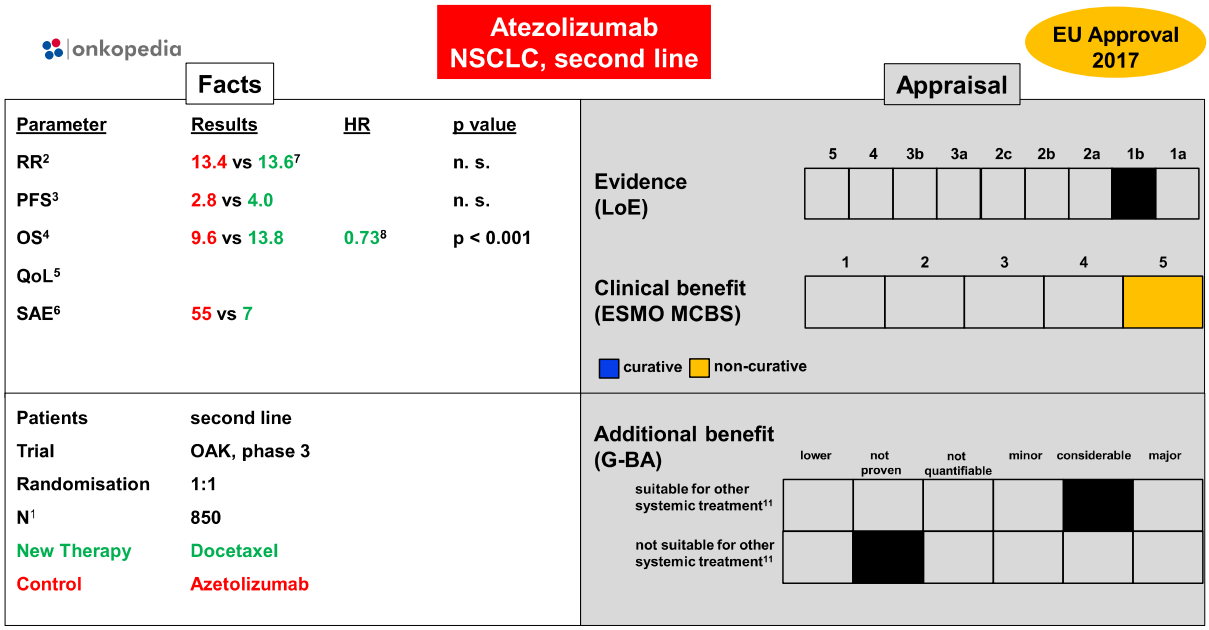


Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months, in %; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy;
Publication: DOI:10.1056/NEJMoa1810865

6.2.2.2.2.3 Second line, Immunotherapy

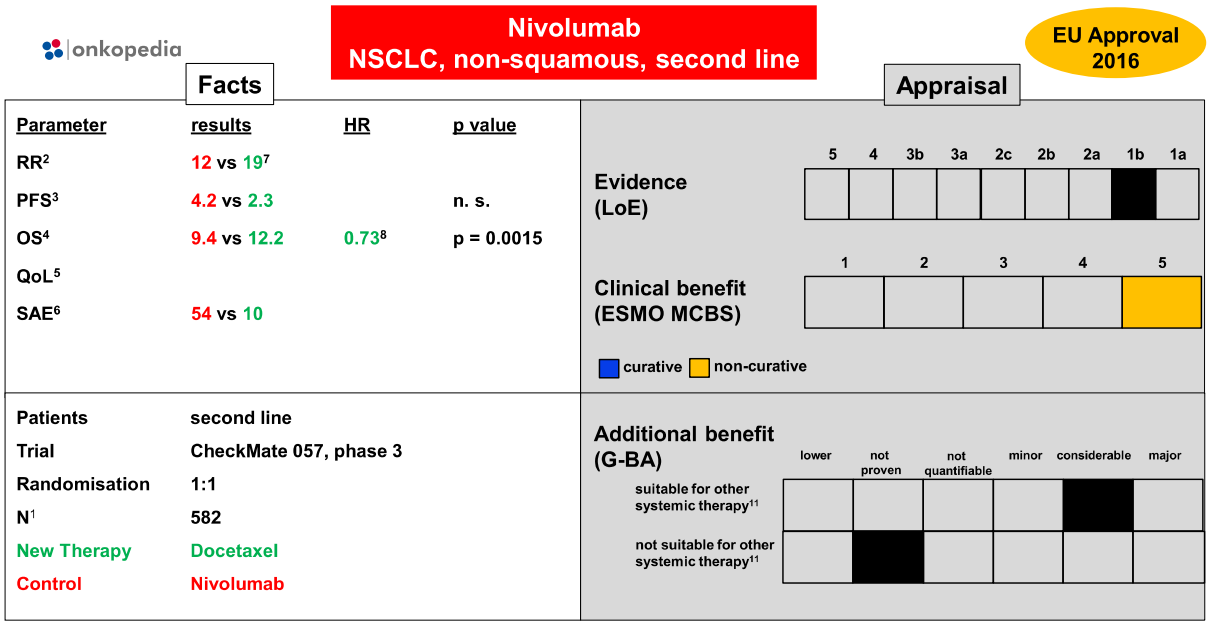
Data are summarized in Figure 33, Figure 34, Figure 35 and Figure 36.

Figure 33: Atezolizumab in NSCLC, second line



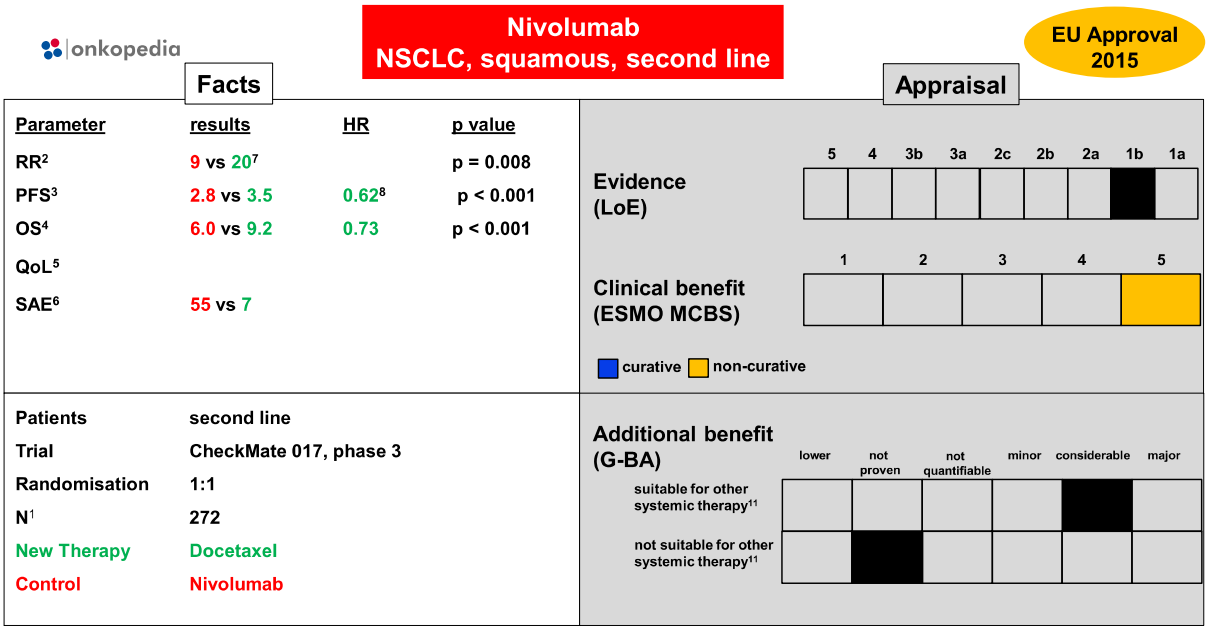
Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months, in %; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [11] docetaxel, pemetrexed or nivolumab;
Publication: DOI:10.1016/S0140-6736(16)32517-X

Figure 34: Nivolumab in NSCLC, non-squamous, second line



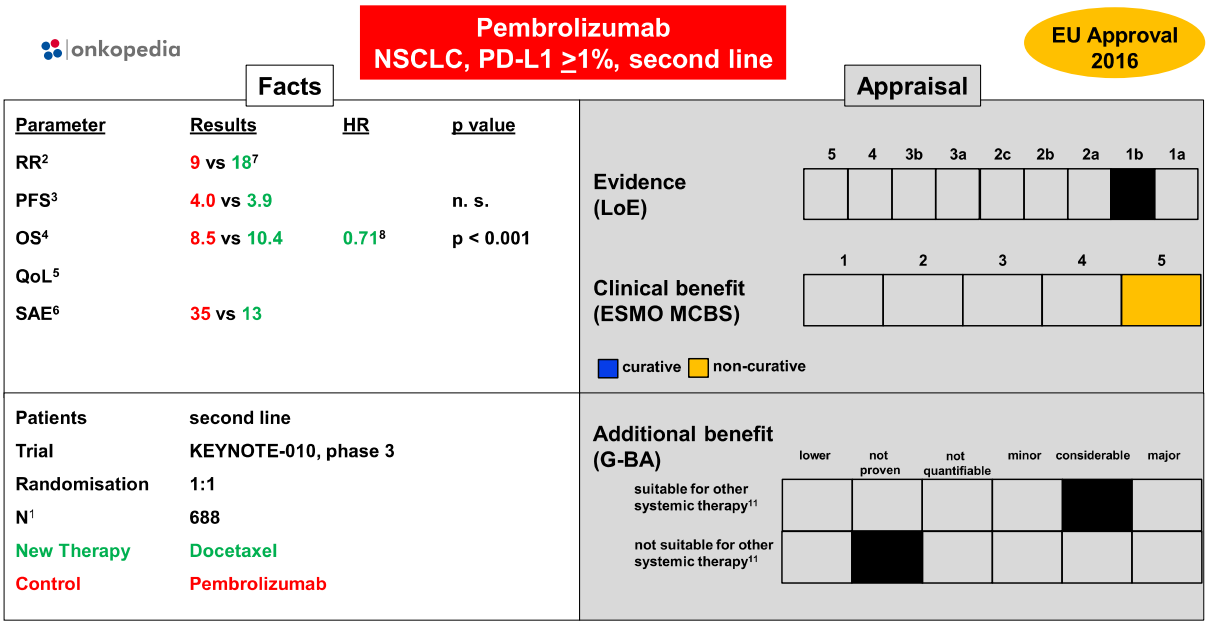
Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months, in %; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [11] pemetrexed, gefitinib or crizotinib;
Publication: DOI:10.1056/NEJMoa1507643

Figure 35: Nivolumab in NSCLC, squamous, second line



Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months, in %; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [11] docetaxel;
Publication: DOI:10.1056/NEJMoa1507643

Figure 36: Pembrolizumab in NSCLC, PD-L1 ≥%, second line



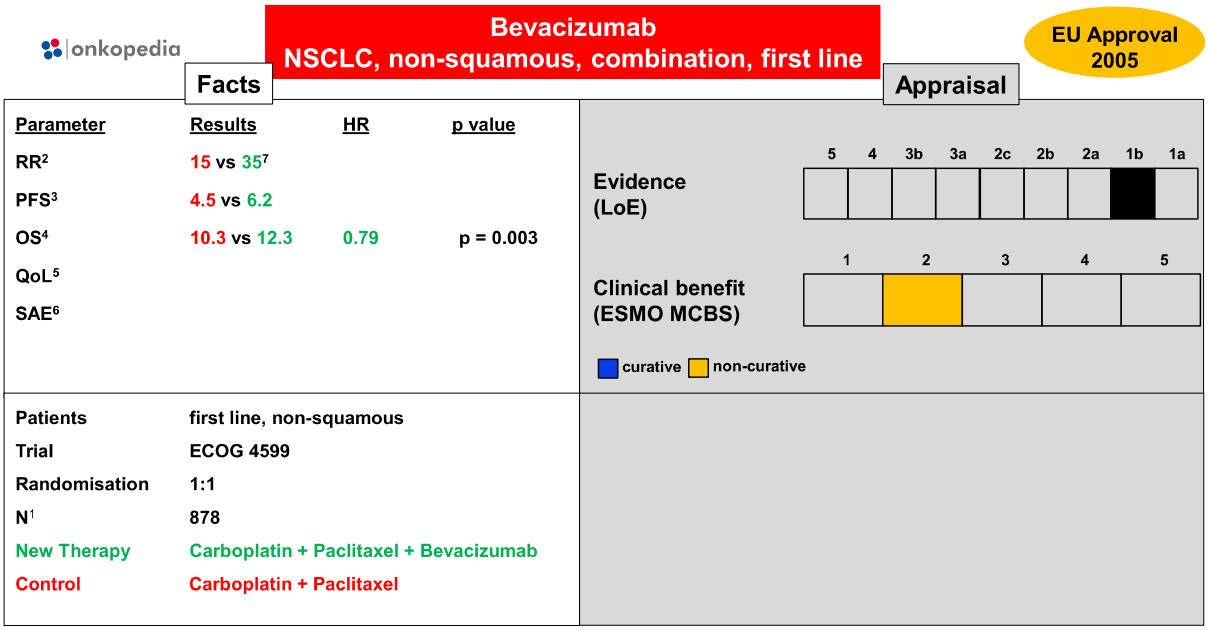
Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months, in %; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [11] pemetrexed, docetaxel or nivolumab;
Publication: DOI:10.1016/S0140-6736(15)01281-7

6.2.2.2.3 Others

6.2.2.2.3.1 First line, others

Data are summarized in Figure 37.

Figure 37: Bevacizumab in NSCLC, non-squamous, combination, first line

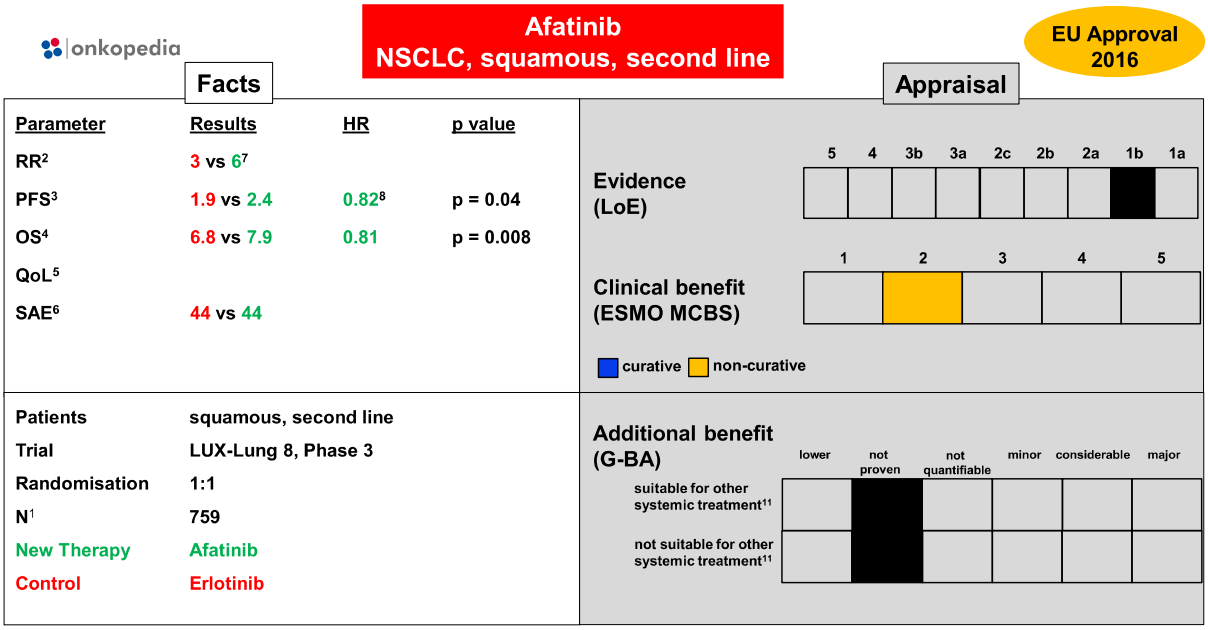


Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months, in %; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy;
Publication: DOI:10.1056/NEJMoa061884

6.2.2.2.3.2 Second line, others

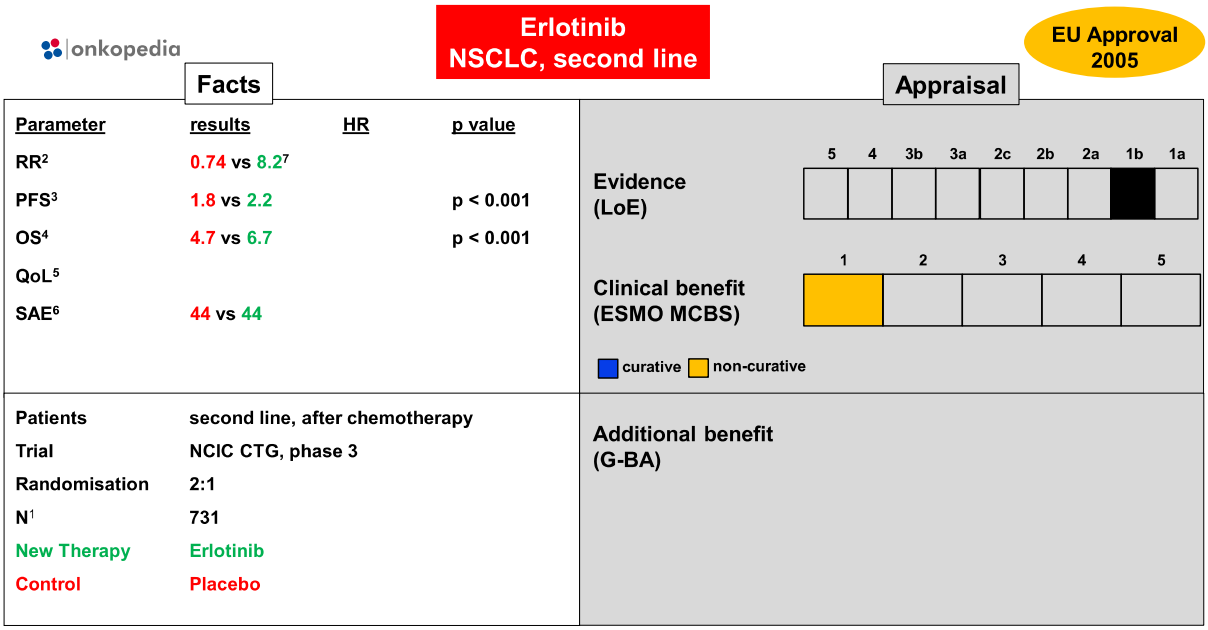
Others including antiangiogenetic agents and tyrosine kinase inhibitors. Data are summarized in Figure 38, Figure 39, Figure 40 and Figure 41

Figure 38: Afatinib in NSCLC, squamous-cell carcinoma, first line



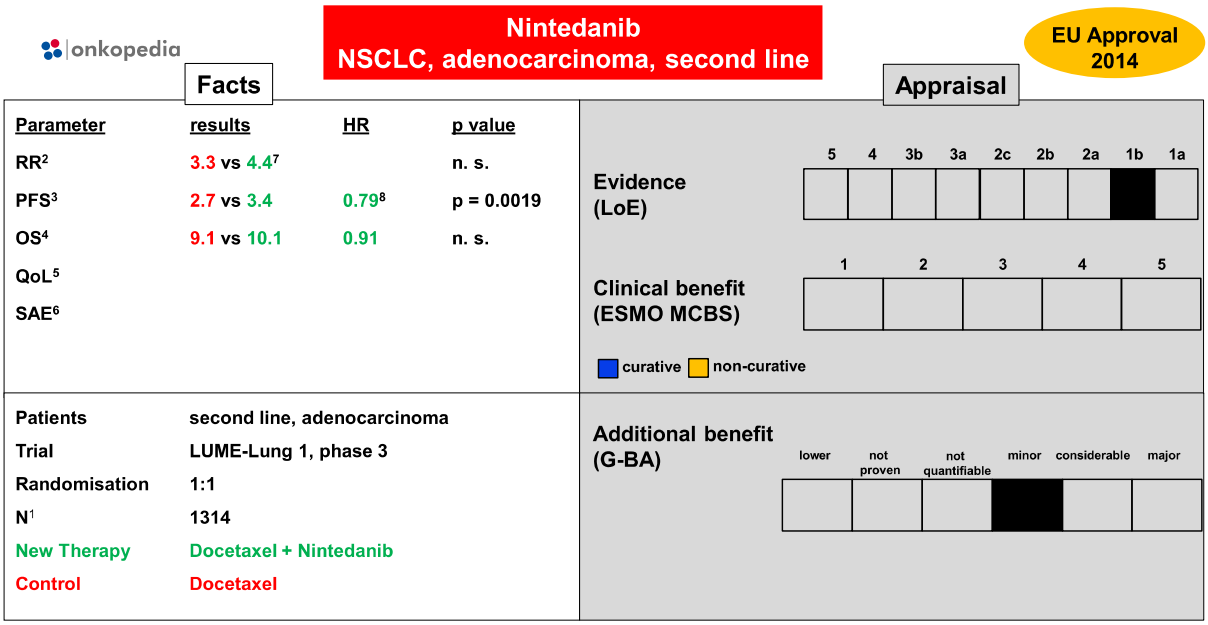
Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months, in %; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy; [11] docetaxel;
Publication: DOI:10.1016/S1470-2045(15)00006-6

Figure 39: Erlotinib in NSCLC, EGFRmut, second line



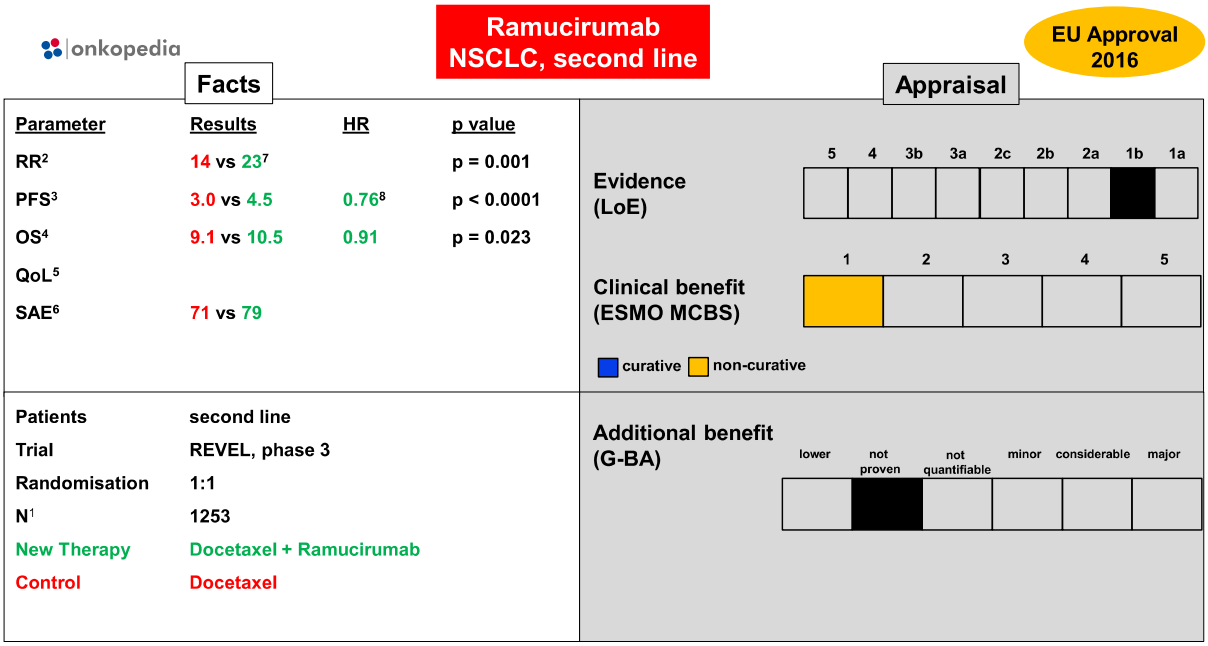
Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months, in %; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy;
Publication: DOI:10.1056/NEJMoa050753

Figure 40: Nintedanib in NSCLC, adenocarcinoma, combination, second line



Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months, in %; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy;
Publication: DOI:10.1016/S1470-2045(13)70586-2

Figure 41: Ramucirumab in NSCLC, combination, second line



Legend:
[1] N - number of patients; [2] RR - remission rate, in %; [3] PFS - progression-free survival, in months; [4] OS – overall survival, in months, in %; [5] QoL – quality of life; [6] SAE – serious adverse events, CTCAE grade 3/4; [7] results for control, results for new therapy; [8] hazard ratio for new therapy;
Publication: DOI:10.1016/S0140-6736(14)60845-X

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15 Disclosure of Potential Conflicts of Interest

according to the rules of the responsible Medical Societies.