| Reference | Tool | QoL | Compliance |
|---|---|---|---|
| Kelly 2001[48] | FACT-L version 3 | With the three categories of improved, stable and declined, there were no statistically significant treatment arm differences in QoL at 13 weeks ($p = 0.97$) or 25 weeks ($p = 0.74$) | QoL initiated halfway through the trial; thus, only 123 patients on the VNB + CIS arm and 122 patients on the PAX + CARB arm could have completed the baseline FACT-L questionnaire. Of this group, 91% of patients submitted a FACT-L questionnaire at baseline. Follow-up submission rates were 68% at 13 weeks and 47% at 25 weeks |
| Scagliotti 2002[43] | EORTC QLQ-C30-LC13 | After two cycles of chemotherapy, only six of the functional and symptom scales of the EORTC QLQ-C30-LC13 showed treatment differences: role functioning (patients' ability to work or participate in leisure activities), fatigue, nausea/vomiting, anorexia, peripheral neuropathy and alopecia<br>Further analysis showed that there were no statistical differences between the GEM + CIS and VNB + CIS arms. However, the PAX + CARB arm differed significantly from the VNB + CIS arm, with role functioning, fatigue, nausea/vomiting and anorexia favouring the PAX + CARB arm, and peripheral neuropathy and alopecia favouring the VNB + CIS arm<br>When the same analysis was conducted after four cycles of therapy, the only scales showing treatment differences were pain, nausea/vomiting, peripheral neuropathy and alopecia. Further analysis showed a statistical difference between the GEM + CIS and VNB + CIS arms in peripheral neuropathy, which favoured the GEM + CIS arm. This analysis also showed statistical differences between the PAX + CARB and VNB + CIS arms for pain, peripheral neuropathy and alopecia, all of which favoured the VNB + CIS arm. Only nausea/vomiting, peripheral neuropathy and alopecia showed sustained treatment differences | Compliance at baseline was high (93–95%), but at later cycles, the percentage of patients still receiving therapy and who completed the questionnaire decreased |
| Schiller 2002[47] | NR | NR | NR |
| Fossella 2003[44] | LCSS and EQ-5D | Patients treated with either DOC + CARB or DOC + CIS reported consistently improved global QoL compared with patients treated with VNB + CIS, who generally experienced a deterioration in QoL. For patients treated with DOC + CARB, this overall advantage in global QoL was statistically significant according to both LCSS ($p = 0.016$) and EuroQol ($p < 0.001$) assessments. For patients treated with DOC + CIS, the advantage in global QoL was statistically significant when evaluated by EuroQol ($p = 0.016$), but not when evaluated by the LCSS ($p = 0.064$) | The baseline EuroQol questionnaire was completed by 831 patients (DOC + CIS, 281; DOC + CARB, 279; VNB + CIS, 271) and 811 patients (DOC + CIS, 279; DOC + CARB, 269; VNB + CIS, 263) completed the baseline LCSS questionnaire |

| Reference | Tool | QoL | Compliance |
|---|---|---|---|
| Gebbia 2003[49] | NR | NR | NR |
| Gridelli 2003[45] | EORTC QLQ-C30 and QLQ-C30 | There were no significant differences in global QoL scores between the two arms (GEM + CIS and VNB + CIS were assessed as one CIS-based arm vs GEM + VNB) after 2 months of treatment. Worsening scores for appetite, vomiting and alopecia were significantly more common in the GEM + CIS and VNB + CIS arms compared with GEM + VNB<br>Baseline mean scores were comparable between the two arms for all of the QoL items. At the planned point for primary QoL analysis (general QoL and health status at the end of cycle 2) no difference was observed between arms ($p = 0.94$); the observed effect size was just 0.06<br>Role and emotional functioning had higher (better) scores with GEM + VNB; at week 1 (corresponding to day 8 of cycle 1), mean changes were always worse in the GEM + CIS and VNB + CIS<br>Loss of appetite, fatigue, vomiting and hair loss were worse in the GEM + CIS and VNB + CIS, across all of the periods, particularly at week 1 for the former three symptoms<br>Slight advantages in cough, shoulder pain and analgesic consumption were seen among patients receiving GEM + CIS and VNB + CIS treatment<br>Overall, in both arms, almost 40% of patients exhibited an improved global QoL and one fourth of patients remained stable. After adjustment for possible confounding variables, significant differences were seen only for appetite, vomiting and hair loss (all symptoms were worse in GEM + CIS and VNB + CIS) | Overall, 209 patients in the PLAT-based arm and 206 patients in the GEM + VNB arm were analysed. There were no differences in any of the compliance parameters between the two study arms. The rate of completed questionnaires, out of on-treatment patients, declined slightly to 84% (172 of 205), 75% (148 of 197), 85% (140 of 165) and 80% (111 of 139) in the PLAT-based arm and to 82% (163 of 199), 81% (157 of 194), 74% (129 of 174) and 74% (110 of 149) in the GEM + VNB arm at assessments made at weeks 1, 3, 6 and 9, respectively |
| Smit 2003[46] | NR | When comparing GEM + CIS with PAX + CIS, no significant difference in global QoL ($p = 0.816$) was observed. A statistically ($p < 0.0001$) and clinically significant overall improvement was observed for peripheral neuropathy and alopecia in GEM + CIS compared with PAX + CIS. Nausea and vomiting increased significantly with time, but at a similar rate in both arms. Clinically relevant improvement was observed for coughing and insomnia in both arms | Compliance at baseline and throughout the active treatment period was >60%, but decreased dramatically at cycle 6 (47 forms received of the 183 forms expected; 25.7%) and for assessments during follow-up. This analysis is, therefore, restricted to the treatment period. There was no significant difference in compliance at the different assessment points between the two experimental arms and the standard arm |

| Reference | Tool | QoL | Compliance |
|---|---|---|---|
| Chen 2004[51] | LCSS | There was no statistically significant difference between the PAX + CIS and VNB + CIS arms, either before or two cycles after treatment, or when the patient went off study. This held true whether scored by the patients (nine items) or by the observers (six items), and included the categories of loss of appetite, fatigue, cough, dyspnoea, haemoptysis, pain, disease severity, daily activity and QoL<br>Loss of appetite and pain were worse after two cycles of treatment in the PAX + CIS arm<br>When considering all the treated patients together, there was a slight, although significant decrease in the scores of all items except haemoptysis | 124 patients (62 patients in each arm) completed the baseline LCSS questionnaire, and after two cycles of treatment and/or after going off study |
| Douillard 2005[53] | NR | NR | NR |
| Martoni 2005[54] | NR | NR | NR |
| Thomas 2006[58] | NR | NR | NR |
| Chen 2007[52] | LCSS | No statistically significant difference in the scales between the DOC + CIS and VNB + CIS arms, either before or after two cycles of treatment, or when the patient went off study, and whether scored by the patients (nine items) or by the observers (six items)<br>Cough and dyspnoea were worse in the VNB + CIS arm before treatment<br>When considering all the treated patients together, there was a slight, but significant, decrease in the scores of all items, except haemoptysis, either after two cycles of treatment or after the patient had gone off study | 89 patients (43 patients in the DOC + CIS arm and 46 in the VNB + CIS arm) completed LCSS questionnaire |
| Helbekkmo 2007[55] | EORTC QLQ-C30 and QLQ-LC13 | There was no difference between the VNB + CARB and GEM + CARB arms with respect to mean change of scores or AUC from baseline to week 17 | Completion of the HRQoL questionnaires was 95% and 98% at baseline and declined to minimum 61% and 60% during the 49-week follow-up for the VNB + CARB and GEM + CARB arms, respectively |
| Langer 2007[56] | NR | NR | NR |
| Ohe 2007[57] | FACT-L Japanese version and the QoL Questionnaire for Cancer Patients Treated with Anticancer Drugs (QoLACD) | No statistically significant difference in global QoL was observed among the four treatment groups | NR |
| Chang 2008[50] | NR | NR | NR |
| Scagliotti 2008[61] | NR | NR | NR |

| Reference | Tool | QoL | Compliance |
|---|---|---|---|
| Gronberg 2009[62] | HRQoL | No clinically relevant differences in mean score between the treatment arms for either of the primary HRQoL end points. The difference in mean score between PEM + CARB and GEM + CARB and the difference in mean score from baseline through the treatment period did not exceed 10 points on any of the scales at any time point. In addition, there were no statistically significant differences in AUC for global QoL ($p = 0.72$), nausea/vomiting ($p = 0.55$), fatigue ($p = 0.55$) or dyspnoea ($p = 0.48$). Furthermore, the sensitivity test did not show any differences in AUC. There were no clinically relevant or statistically significant differences between the treatment arms on the other HRQoL scales, although there was a trend to better physical functioning and less alopecia on the PEM + CARB arm | Patients completed 2017 (87%) of 2310 HRQoL questionnaires (deceased patients excluded) during the first 20 weeks. Compliance was similar in the two groups (PEM + CARB: 98% to 80%, GEM + CARB: 99% to 78%) |
| Mok 2009[15] and Fukuoka 2011[64] | FACT-L and TOI | Significantly more patients in GEF than in PAX + CARB had a clinically relevant improvement in QoL (odds ratio 1.34; 95% CI 1.06 to 1.69; $p = 0.01$) and by scores on the TOI (odds ratio 1.78; 95% CI 1.40 to 2.26; $p < 0.001$). Rates of reduction in symptoms were similar between GEF and PAX + CARB (odds ratio with GEF 1.13; 95% CI 0.90 to 1.42; $p = 0.30$) | NR |
| Tan 2009[59] | LCSS | No significant difference between the two arms for appetite, asthenia, cough, dyspnoea, haemoptysis and pain. The average symptom burden as assessed by the LCSS was similar in the two arms. The global score was similar in DOC + CIS and VNB + CIS arms, showing a worsening from baseline to cycle 6 relative to the disease evolution | 149 patients in the VNB + CIS arm (78.4%) and 152 patients in the DOC + CIS arm (79.6%) were assessable for the QoL LCSS questionnaire |
| Maemondo 2010[63] | NR | NR | NR |
| Mitsudomi 2010[65] | NR | NR | NR |

NR, not reported.