*Table 3. Patient characteristics*

| | | INH IL-2 treatment (n = 75) | SYST IL-2 treatment (n = 202) |
|---|---|---|---|
| Age | (years) | | |
| | Mean | 58 | 57 |
| | Median | 58 | 57 |
| | Range | 28–75 | 35–75 |
| Gender | | | |
| | Male (n, [%]) | 56 [75] | 143 [71] |
| Nephrectomy | | | |
| | Yes (n, [%]) | 70 [93] | 167 [83] |
| Types of metastases (n [%]) | | | |
| | Lung only | 29 [39] | 75 [37] |
| | Lung and other metastases | 46 [61] | 127 [63] |
| Prior chemotherapy (n, [%]) | | 4 [5] | 13 [6] |
| Prior radiotherapy (n, [%]) | | 5 [6] | 38 [19] |
| IL-2 treatment (n, [%]) | | | |
| | Monotherapy | 45 [60] | 64 [32] |
| | Combinated therapy with IFN-α | 30 [40] | 138 [68] |
| Risk factors | | | |
| | ECOG status (n, [%]) | | |
| | 0 | 4 [5] | 91 [45] |
| | 1 | 64 [86] | 111 [51] |
| | 2 | 7 [9] | 9 [4] |
| Diagnosis-to-treatment interval (months) | | | |
| | Mean | 29 | 24 |
| | Median | 10 | 8 |
| | Range | 0–163 | 0–199 |
| | < 24 months (n, [%]) | 51 [68] | 144 [71] |
| | > 24 months (n, [%]) | 24 [32] | 58 [29] |

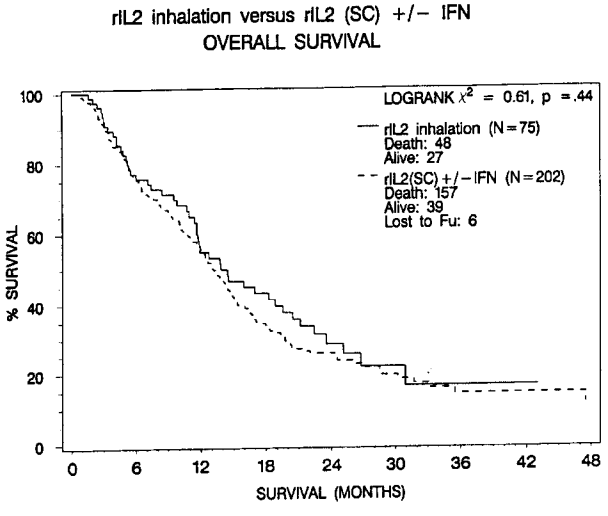


*Fig. 1.* Kaplan-Meier survival analysis of patients with metastatic renal cell carcinoma treated with INH or SYST IL-2. Abscissa: survival time (months). Ordinate: percentage of surviving patients. Fu – follow-up.

### *Patient survival*

A Kaplan-Meier curve depicting the survival of patients treated with INH IL-2 versus SYST IL-2 is presented in Fig. 1. Univariate analysis of patient survival revealed that patients treated with INH IL-2 versus SYST IL-2 had comparable survival times. The median survival time was 13.8 months for those patients receiving INH IL-2 therapy, and 13.1 months for patients receiving SYST IL-2 therapy ($X^2 = 0.61$; $P = 0.44$). The one-year survival rates were 55% and 56% for patients treated with INH IL-2 and SYST IL-2, respectively. At two years, survival rates were 28% for the patients receiving INH IL-2 and 26% for the patients receiving SYST IL-2.

Multivariate analysis of patient survival using Cox's proportional hazards model was also performed, and the results are summarized in Table 6. Results of this analysis revealed that patients had a similar likelihood of survival whether they were treated with INH IL-2 or SYST IL-2 (risk ratio = 0.81, P = 0.23), and whether or not they had undergone a nephrectomy (risk ratio = 0.99, P = 0.97).

*Table 4. Objective responses of patients with metastatic renal cell carcinoma to INH or SYST IL-2 treatment*

| Treatment group | Complete response n (%) | Partial response n (%) | Stable disease n (%) | Progressive disease n (%) |
|---|---|---|---|---|
| INH IL-2 (n = 75) | 1 (1.3) | 7 (9.4) | 37 (49.3) | 30 (40.0) |
| SYST IL-2 (n = 202) | 9 (4.4) | 36 (17.8) | 71 (35.1) | 79 (39.1) |

*Table 5. Objective responses of patients with metastatic renal cell carcinoma to treatment with INH or SYST IL-2 as a function of ECOG performance status*

| ECOG-performance status score | Complete response n (%)* | Partial Response n (%)* | Stable disease n (%)* | Progressive disease n (%)* |
|---|---|---|---|---|
| **INH IL-2 treatment (n = 75)** | | | | |
| 0 (n = 4) | - | 1 (25.0) | 2 (50.0) | 1 (25.0) |
| 1 (n = 64) | 1 (1.6) | 6 (9.4) | 32 (50.0) | 25 (39.0) |
| 2 (n = 7) | - | - | 3 (42.9) | 4 (57.1) |
| **Systemic IL-2 treatment (n = 202)** | | | | |
| 0 (n = 91) | 7 (7.7) | 20 (22.0) | 36 (39.6) | 27 (29.7) |
| 1 (n = 102) | 2 (2.0) | 15 (14.7) | 32 (32.4) | 47 (46.1) |
| 2 (n = 9) | - | 1 (11.1) | 2 (22.2) | 5 (55.6) |

*Percentages reflect the proportion of patients relative to the number of patients in the treatment group having a particular ECOG status score.

*Table 6. Multivariate analysis of patient survival**

| Variable | $X^2$ | P-value | Risk ratio** | 95% CI |
|---|---|---|---|---|
| INH IL-2 therapy | 1.44 | 0.23 | 0.81 | 0.57–1.14 |
| Nephrectomy | 0.0013 | 0.97 | 0.99 | 0.67–1.48 |
| Risk factors | | | | |
| ECOG performance status 1 or 2 | 5.65 | 0.02 | 1.47 | 1.07–2.02 |
| DTI $\leq$ 24 months | 18.8 | 0.0001 | 2.12 | 1.51–2.98 |
| Lung metastases only | 14.2 | 0.0002 | 0.54 | 0.40–0.767 |

*Using Cox's proportional hazards model
**Interpreted relative to the characteristics of the reference patients, i.e., SYST IL-2 therapy, no nephrectomy, ECOG performance status = 0, DTI > 24 months, and lung and other metastases, respectively

However, patients with risk factors had a significantly lower likelihood of survival than patients without these risk factors. In this regard, patients with a poorer performance status (ECOG performance score of 1 or 2) were at significantly greater risk than patients with an ECOG performance score of 0 (risk ratio = 1.47, P = 0.02). Furthermore, patients characterized by a diagnosis-to-treatment interval of $\leq$ 24 months were at more than twice the risk of patients with a diagnosis-to-treatment interval of > 24 months (risk ratio = 2.12, P = 0.0001). Additionally, patients with lung metastases only were at almost half the risk of patients who had lung and other metastases (risk ratio = 0.54, P = 0.0002).

### *Treatment-related toxicity*

The proportion of patients experiencing toxicity related to INH IL-2 or SYST IL-2 treatment is summarized in Table 7. Although both treatment groups experienced toxicity with the therapy, the group receiving INH IL-2 treatment experienced substantially less toxicity than the group receiving SYST IL-2 treatment. Similar proportions of patients in the two treatment groups experienced Grade 1 and Grade 2 toxicities. However, 24% of patients treated with INH IL-2 versus 46% of patients treated with SYST IL-2 experienced Grade 3 toxicities. Furthermore, no patients receiving INH IL-2 treatment experienced Grade 4 toxicities, but 3% of patients receiving SYST IL-2 experienced such toxic events.

For patients receiving INH IL-2 treatment, the most common adverse event experienced was cough, which could be controlled by administering an antitussive agent. All patients treated with INH IL-2 required some form of medication to treat local irritation associated with INH therapy (e.g., cough suppressants or $\beta_2$-adrenergic sympathomimetic agents [bronchodilators]). Patients did not receive medications for the prophylactic treatment of side effects, but did receive such medications as needed during INH IL-2 therapy. Notably, 50% of patients receiving