We evaluated the efficacy, compliance, and side effects of anti-androgen monotherapy vs. LHR agonists in patients with localized prostate cancer ineligible for definitive local therapy. The records of 62 patients who received exclusively either anti-androgen monotherapy or LHR agonists (Lupron) were reviewed. PSA levels, Gleason scores, clinical stage, and side effects were recorded. Of the 62 study patients, 37 received LHRH agonists (Lupron) and 25 received anti-androgen monotherapy (Casodex = 16, Nilandron = 6, Eulexin = 3). The mean follow-up was 12.79 ± 1.2 months in the anti-androgen group and 30.82 ± 3.73 in the Lupron group (P=<0.001). The mean Gleason scores were 5.84 ± 0.43 and 5.95 ± 0.42 (P=0.15), respectively. The mean initial PSA values were 13.52 ± 4.12 and 14.24 ± 2.12 (P=0.45). A higher percent decline in PSA was seen in the Lupron group (96.6 ± 3.0) than in the anti-androgen group (85.2 ± 5.5; P=<0.001). Only one patient in the Lupron group broke through PSA nadir (2.7%), whereas 8 patients (32%) in the anti-androgen group broke through their nadir (P = 0.002). Compliance for the Lupron group was 100% (37/37) whereas it was 96% (24/25) in the anti-androgen group. However, 28% of the patients switched from one anti-androgen to another. Lupron appears to be a better alternative than anti-androgens in the long-term control of localized prostate cancer. Anti-androgen monotherapy appears to be better suited for short-term suppression.