CHAPTER I

INTRODUCTION

Rationale and Background

Cervical cancer is the worldwide third most common cancer in women.[1] However, in the developing countries including Thailand, this cancer is still one of the leading causes of death. In addition, most of the new cases present with advanced stages[2], likely because of poor access to screening programs. The most important determinant of prognosis remains clinical staging, which is defined by tumor volume and extend of disease spread. The overall 5-year survival rate ranges from 95-100% in stage IA to 75-90% in stage IB disease, while patients with in stage IIB-IVA or locally advanced disease which treated with concurrent chemo-radiation (CCRT), have 5-year survival rate about 50-60%. Patients with stage IVB disease have a $\leq$ 5% chance of surviving 5 years after diagnosis.[3] The majority of Thai patients are in locally advanced stage.[4] While in the United State of America, the grater number of patients are in the early stage due to their better screening system.[5]

Squamous cell carcinoma (SCC) is the most common histology of invasive cervical cancer, which accounts for approximately 80% of all carcinomas of the uterine cervix. SCC is composed of cores and nests of epithelial cells arranged randomly; cells show central keratinization with cornified pearls and sometimes necrosis. Nonkaratinizing tumors may be seen. SCC is divided into three types: large cell keratinizing and nonkeratinizing and small cell type and they are subdivided according to the degree of differentiation into well, moderately, or poorly differentiated. Most reports have shown no significant correlation of survival or tumor behavior with degree of differentiation of SCC. For the most part, the decline in the annual incidence of invasive cervical carcinoma has been seen primarily among patients with subtype. In the past, adenocarcinoma (ACA) was relatively uncommon as a histology of cervical cancer. This cell type arises from the cylindrical mucosa of the endocervix or the mucous secreting endocervical glands. Mucinous is the most common substage of ACA. Due to ACA arises from endocervix, Pap smear may be not detected some of diseases. As a result of the decrease in the overall incidence of invasive SCC and increase in the baseline incidence of ACA, this histology now accounts for approximately 20% of all cervical cancer.[3]

Controversy exists as to whether histological type is an independent prognostic factor for survival.[3,6] Although some studies have shown no difference in survival between ACA and SCC,[7,8] the majority have shown that ACA carries a worse prognosis with 10-20% difference in 5-year overall survival rates.[9-11] The poorer prognosis associated with ACA may be due to the relatively higher frequency of late stage at the time of diagnosis among patients with this histological type. In several series in which patients were stratified by stage and tumor size, the outcome of cervical ACA

appeared to be similar to that of squamous lesions of the cervix.[3] Due to small proportions of patients with ACA histology, specific level 1evidence to guide patient management is lacking. Most trials have included ACA but in insufficient numbers to do more than generate hypotheses from subset analysis. Therefore, most of knowledge on the treatment of cervical cancer comes from studies where the majority of the patients had SCC. Very few studies reported separate treatment outcomes of ACA and compared them with SCC, especially in locally advanced stage. Furthermore, not all of these comparative studies have included ≥ 100 ACA patients .[7,9-11] As a result, our understanding of the natural history and optimal management of locally advanced cervical cancer patients with ACA are limited.